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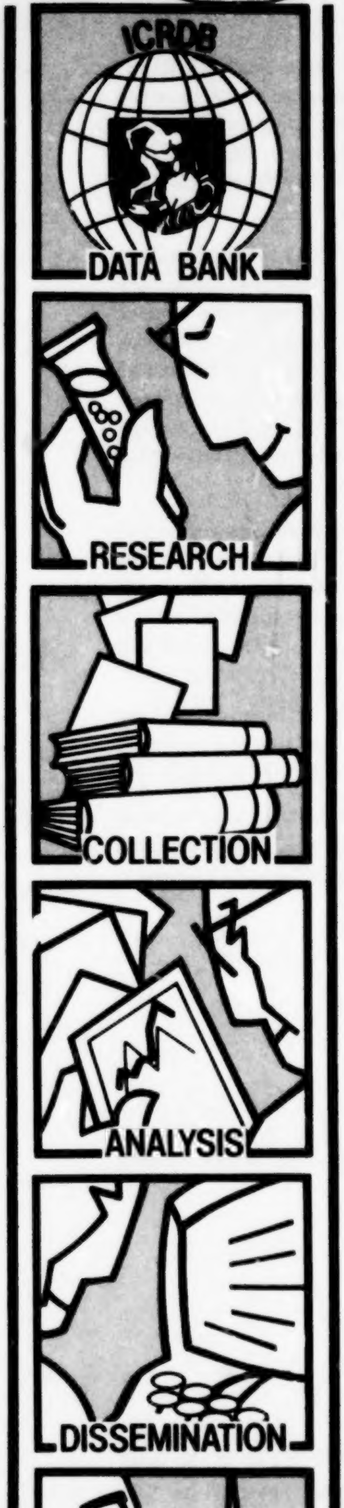
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ONCOLOGY OVERVIEW

SELECTED ABSTRACTS

ON

ORGAN SPECIFIC CARCINOGENICITY OF TOBACCO PRODUCTS: EPIDEMIOLOGY OF NON-RESPIRATORY TRACT CANCER AND RELATED CLINICAL OBSERVATIONS

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Selected Abstracts

On

ORGAN SPECIFIC CARCINOGENICITY OF TOBACCO PRODUCTS: EPIDEMIOLOGY OF NON-RESPIRATORY TRACT CANCER AND RELATED CLINICAL OBSERVATIONS

Dietrich Hoffmann, Ph.D.; Ilse Hoffmann
Consulting Reviewers

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of the National Cancer Institute**

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INTRODUCTION

This ONCOLOGY OVERVIEW on the organ specific carcinogenicity of tobacco products (cancer epidemiology of non-respiratory tract cancer and related clinical observations) includes abstracts selected from the CANCERLINE data base, referencing articles published mainly during 1975-1979. A few key references from the 1960's have been included for historical perspective. The strategy used for the on-line data base search is available upon request from the CIDAC office and can be entered at any MEDLARS/MEDLINE terminal system, with minor modifications, in order to obtain updates in this area.

The scope of the OVERVIEW covers all epidemiological aspects of the association of human non-respiratory tract cancers with the consumption of tobacco products and selected clinical observations relevant to the etiology of these cancers. The organ sites covered include the oral cavity, the esophagus, the stomach, the pancreas and the urinary tract. Selected abstracts on other organ sites are also included. The histopathological and cytological effects of tobacco in man are also covered. This OVERVIEW includes observations indicating the interaction of tobacco products with other possible cofactors of human cancer. This OVERVIEW excludes studies pertaining only to the diagnosis or therapy of tobacco-related cancers. Experimental studies tobacco-related carcinogenesis are the subject of a separate, complementary ONCOLOGY OVERVIEW, Organ Specific Carcinogenicity of Tobacco Products: Bioassays, Physicochemical Analysis, and Other Experimental Evidence.

This OVERVIEW was prepared by Dietrich Hoffman, Ph.D., and Ilse Hoffman of the American Health Foundation, and Michael Feldman, M.S., of the CIDAC for Carcinogenesis Information, The Franklin Research Center.

EDITORIAL COMMENTARY

It is now widely accepted that cigarette smoking is causally associated with cancer of the lung and larynx. It is less widely known that cigarette smokers also face an increased risk for cancer of the oral cavity, esophagus, pancreas, kidney and urinary bladder. Smoking of pipes and cigars, as well as tobacco chewing, are correlated with cancer of the mouth and esophagus. A few studies have suggested an association between tobacco usage in the form of snuff and cancer of the nasopharynx.

The first clinical observation suggesting tobacco smoke as a possible carcinogen was published by Sommering in 1792 (1). The German physician pointed to carcinoma of the lip as a consequence of pipe smoking. The occurrence of cancer of the mouth in Indian men who chew a mixture of areca nut, lime and tobacco has been known for more than a century (2). In 1920 the American physician Broders noted that among 526 male and 11 female patients with epithelioma of the lip, 80.5% were tobacco users (3). The first epidemiological study linking carcinoma of the urinary tract and cigarette smoking was conducted by Lilienfeld et al on 324 male and 116 female patients (4). In 1966, prospective studies by Hammond (5) and by Dorn (6) reported an increase of pancreatic cancer among cigarette smokers. The early findings on tobacco usage and cancer of the mouth and esophagus, as well as the observations linking cigarette smoking to cancer of the pancreas, kidney and urinary bladder have since been supported by more than one hundred epidemiological studies.

Cancers of the mouth and of the esophagus are generally considered to result from long term direct contact of the epithelial tissues with the carcinogens and cocarcinogens in tobacco juices and smoke. Excessive alcohol consumption and/or nutritional deficiencies, including zinc deficiency, most likely accelerate neoplastic processes induced in these tissues by tobacco smoke constituents. Numerous experimental studies support these hypotheses and continue to produce evidence of organ-specific carcinogens. The accumulation of epidemiological, clinical and experimental evidence of neoplastic responses to organ-specific carcinogens is reflected in an ever increasing volume of scientific literature.

The subject of Organ-Specific Carcinogenicity of Tobacco Products is covered by means of two separately published and complementary ONCOLOGY OVERVIEWS:

1. Epidemiology of Non-Respiratory Tract Cancer and Related Clinical Observations
2. Bioassays, Physicochemical Analysis, and Other Experimental Evidence

REFERENCES

1. Sommering, S.T.: De Morbis Vasorum Absorbentium Corporis Humani, Varrentrapii et Wenneri, Traiecti and Moenum (Frankfurt, Main, Germany) 1792, p 109.

2. Kanolkar, V.R.: Cancer in India in Relation to Habits and Customs. In: "Cancer" Vol. 3, R.W. Raven, ed. pp. 272-280. Butterworth and Co., London, 1958.

3. Broders, A.C.: Squamous-cell Epithelioma of the Lip. J. Am. Med. Assoc. 74: 656-664, 1920.

4. Lilienfeld, A.M., Levin, M. and Moore, G.E.: The Association of Smoking With Cancer of the Urinary Bladder in Humans. Am. Med. Assoc. Arch. Intern. Med. 98: 125-135, 1956.

5. Hammond, E.E.: Smoking in Relation to the Death Rates of One Million Men and Women. Natl. Cancer Inst. Monogr. 19: 127-204, 1966.

6. Kahn, H.A.: The Dorn Study of Smoking and Mortality Among U.S. Veterans. Report on Eight and One-half Years of Observation. Natl. Cancer Inst. Monogr. 19: 1-125, 1966.

I. CANCER OF THE ORAL CAVITY

A. Epidemiological Studies of Tobacco-Related Oral Cancer

EDITOR'S NOTE: Additional epidemiological studies which concern the association of smoking with oral cancer have been listed under subsequent headings of Section I, because they emphasize specific factors such as alcohol consumption, tobacco and/or betel nut chewing, or reverse smoking.

Section VII lists comparative epidemiological studies dealing with multiple cancer sites, including the oral cavity.

1. EPIDEMIOLOGY OF ORAL CANCER.

Sellars SL
Dept. Otolaryngology, Medical Sch., Univ. Cape Town, Cape Town, S. Africa 7925
Otolaryngol Clin North Am; 12(1):45-55 1979

Worldwide incidences and etiological factors associated with oral cancer (OC) are reviewed. In most Western countries, the incidence of OC in men has declined over the past 20 yr, a trend attributable to changes in smoking and chewing habits, improved oral hygiene, eradication of dietary deficiencies, and effective treatment of syphilis. In some of these countries, the incidence has increased in women. There is a 30-fold variation in the OC incidence rate among different countries. Eighty percent of patients are greater than 50 yr old and, except in India, 70%-80% are men. The high incidence of OC among Indian women has been attributed to the habit of betel chewing: 70% of Indian women but only 10% of the men chew betel. The traditional list of etiological factors includes syphilis, sepsis, alcohol, and tobacco. Recent additions are trauma, infection, and dietary deficiencies. Under conditions of poor oral hygiene, secondary infections occurs at traumatized sites, followed by chronic inflammatory mucosal hyperplasia. This tissue reaction also results from dentures. In one age-matched series, OC was twice as common in the edentulous. Two infections, candidiasis and herpes, have been linked to OC. Iron deficiency has been specifically related to cancer of the mouth, pharynx, and esophagus. Although long-standing malnutrition is related to mucosal atrophy and to leukoplakia, OC is not more common among the chronically malnourished peoples of the world. (3 Refs)

2. SMOKING AND ORAL PATHOLOGY: AN EPIDEMIOLOGIC STUDY.

Taubenhaus LJ, Maloof EC, Scanlon JW
Dept. Public Health, Brookline, Mass.
J Am Geriatr Soc; 12(9):871-876 1964

In a study of 1,108 adults (age 24-91 yr) screened in the oral cancer detection clinic of the Brookline Health Depatient, 126 had oral pathology: 27 (2.4%) high cancer-risk lesions; 6 were malignant (occurrence rate = 5.4/1,000) including 5 squamous cell carcinomas of the buccal mucosa and 1 epidermoid lip carcinoma. The age distributions in the normal and abnormal groups were similar, the largest number of patients being in the 60-69 decade, although the median age for the abnormal group was 10 yr higher. Abnormal males were most numerous in the 50-59 and females in the 60-69 decade. Male smokers were 3x more frequent than female smokers in both groups. Smoking habits in relation to clinical findings showed that among smokers 433 (86%) were normal and 72 (14%) were abnormal; among nonsmokers 549 (91%) were normal and 54 (9%) were abnormal. Of the patients with abnormal findings, 25% smoked more than 1 package of cigarettes daily, compared with 12% of patients with normal findings. The percentages for those who smoked less than 1 package of cigarettes daily, cigars, or pipes, were the same in both abnormal and normal groups. Biopsies of patients with abnormal findings revealed 19 smokers and 8 nonsmokers, with premalignant or malignant lesions and 52 smokers and 47 nonsmokers with neither type of lesion. Neither the use of dentures or alcohol, nor a family history of cancer appeared to be similarly related to the presence of oral abnormalities.

3. CIGARETTE SMOKING AND CANCER OF THE MOUTH, PHARYNX, AND LARYNX: A CONTINUING STUDY.

Moore C
U. Louisville Sch. Med., Ky.
JAMA; 218(4):553-558 1971

This is the second part of a long term study concerning the effects of continued smoking on the recurrence of laryngeal, pharyngeal and oral cancers; the death risk of patients with a three to eighteen year history of control of such cancers was also examined. The 203 patients with histories of smoking were divided into two groups, one which continued to smoke and one which did not. All patients were followed for seven years. Of the patients who continued to smoke, 40% acquired second cancers in tissues exposed to tobacco smoke. Only 6% of ex-smokers acquired second cancers. The death rate in patients who continued to smoke was twice that of the ex-smokers. The death rate increased sharply after four or five years in the smoking populations. That of the ex-smokers showed a random pattern. These results support previous evidence implicating the use of tobacco in the origin of cancers of the mouth and throat and showing that cessation of smoking is associated with a reduced risk of second cancers.

4. SNUFF AND CANCER OF THE ORAL CAVITY.

Axell T, Mornstad H, Sundstrom B
Institutionen for oral kirurgi, Lunds universitet, S-214 21 Malmo, Sweden
Lakartidningen; 75(22):2224-2226 1978

The relationship between snuff and oral cancer was studied in a series of 375 oral cancer patients found in Sweden during 1962-1971. Forty-one patients admitted using snuff at the time of diagnosis, 8 had been snuff-dippers, 18 denied ever using snuff, and 109 admitted using tobacco in other ways; there were no data on tobacco use for 199 patients. A relationship between snuff and cancer was documented in 14 cases and found probable in 19. In 67.3% of the verified snuff-dippers, the cancer was localized to regions of the oral cavity where the snuff had been placed. Most patients, both the entire group and the snuff-dippers, were in the age bracket 71-80 yr. The percentage of snuff-related tumors increased with advancing age. The findings indicate that snuff-dipping increases the cancer risk at the site where the snuff is placed five- to sixfold. However, this risk is small, especially when it is compared with the relationship between lung cancer and smoking. (7 Refs)

5. GEOGRAPHY OF CANCER.

Blot WJ
Environmental Epidemiology Branch, NCI, Bethesda, MD 20014
Sciences (NY); 17(8):12-15 1977

Cancer incidence varies greatly among populations in different areas of the world. Epidemiologic associations discussed include sunlight and skin cancer; industry, smoking, and lung cancer; snuff use and oral cancer; esophageal cancer, race, and diet; breast cancer and diet; and colon cancer, industrialization and diet. (no Refs)

6. EPIDEMIOLOGICAL STUDIES OF ORAL CANCER.

Pindoorg JJ
Div. Virology, Bureau Biologics, Dept. Oral Pathology, Royal Dental Coll., Food and Drug Admin., NIH, Bethesda, MD, 20014
Int Dent J; 27(2):172-178 1977

A review of data on oral cancer epidemiology indicates that it is characterized by marked geographic differences. In Norway, lip cancer is 20 times more frequent among men than women, and occurs with a double frequency in rural areas compared with cities. Cancer of the tongue occurs with the same frequency in men and women. Oral cancer incidence rates increase sharply with age, especially for men. In a series of seven Western countries, Canada has the highest incidence of cancer of the lip, but within Canada there are marked differences. Regional differences in lip cancer incidence within Czechoslovakia have been explained by more UV radiation more spicy food, and pipe smoking with a short-stemmed pipe. There is a high relative frequency of oral cancer in most countries of Southeast Asia. In Singapore, both male and female Indians and Pakistanis have much higher incidence rates than the other ethnic groups (Chinese, Malays, Europeans). This difference is likely due to the chewing of tobacco together with betel nut and also the occurrence of oral submucous fibrosis. Most of the studies dealing with the etiology of oral cancer have implicated tobacco usage. (16 Refs)

7. EPIDEMIOLOGY AND ETIOLOGY OF ORAL CANCER IN BRITAIN.

Binnie WH
Dept. Oral Medicine and Pathology, Guy's Hosp., London SE1X9RT, England
Proc R Soc Med; 69(10):737-740 1976

The epidemiology and etiology of oral cancer in the United Kingdom are discussed. Malignant neoplasms of the oral tissues account for 2% of all malignant tumors, with the vast majority (90%) being squamous cell carcinomas. About 2,400 new cases and 1,200 deaths are registered each year. Neoplasms arising in the tongue, the rest of the mouth, and the oral mesopharynx carry a much worse prognosis than lip cancers. Lip and intraoral cancer is more common in men than in women. In the last two decades, however, male deaths have decreased from 1,200 to 550, but female deaths have remained constant at 300/yr. The incidence rates for men also decreased over a 10-yr period, 1960-1970, but the incidence in women has remained constant. The majority (98%) of cases of oral cancer are in persons over 40. The lower lip is the most common site for oral cancer and the tongue the most common intraoral site. Stage and site are extremely important factors in determining the chance of survival. An early cancer of the lip has an 83% chance of surviving 5 yr, but a late stage of intraoral lesion has only a 17% chance. Factors such as tobacco (smoking and chewing), alcohol, syphilis, dental sepsis, and iron deficiency have been examined as causes with generally equivocal results. There is a definitive relationship between squamous cell carcinoma of the lower lip and actinic radiation. There would also appear to be a positive association between pipe and cigar smoking and mouth cancer, but a negative one with cigarette smoking. In Britain the increase in alcohol consumption corresponds with the downward trend in oral cancer while in France and the US the increase in alcohol consumption corresponds with an increase in such cancers. It is speculated that this contrast may be due to the prohibition in the United Kingdom of unmatured pot-still spirits containing toxic byproducts which might be a preventive measure in oral carcinogenesis. (15 refs)

8. CELLULAR TYPES, SURVIVAL, RACE, NATIVITY, OCCUPATIONS, HABITS AND ASSOCIATED DISEASES IN THE PATHOGENESIS OF LIP CANCERS.

Keller AZ
VA Cent. Office, Washington, D. C.
Am J Epidemiol; 91(5):486-499 1970

The study group included 314 men with carcinomas of the lip and 2 control groups of equal size (men with carcinomas of the oral and pharyngeal mucous membranes, and men with other diseases), comprising a 20% sample of all males discharged from VA hospitals throughout the U. S during 1958-1962. The group of patients with lip cancer included 3 Negro men (1.0%; compared to 12.8% of the general control group). For the 311 white patients, the annual prevalence rate/100,000 living male veterans (as of 1960) was 1.57. Less than 5% of the 294 squamous cell carcinomas, but 9/16 basal cell carcinomas, involved the upper lip. All 31 tumors which had metastasized (30 squamous cell and 1 basal cell) involved the lower lip. Among the white patients, lip cancer was significantly associated with native residence in the South or emigration from the South to the Rocky Mountain region (especially Arizona and New Mexico); with pipe, cigar and cigarette smoking (although no significant association between lip cancer and pipe smoking alone was found); and with outdoor occupations such as farming. Lip cancers were also strongly associated with cancers of the environmentally-exposed skin (head, face and neck). The lip cancer risk increased with age, but lip cancer was not an important contributor to the causes of death.

9. RISK FACTORS IN LIP CANCER: A QUESTIONNAIRE SURVEY.

Lindqvist C
Finnish Cancer Registry, Liisankatu 21 B, 00170 Helsinki 17, Finland
Am J Epidemiol; 109(5):521-530 1979

An analysis was made of potential risk factors for lip cancer in Finland. The series comprised 290 patients with epidermoid carcinoma of the lip and 254 controls with squamous cell carcinoma of the skin of the head and neck, all reported to the Finnish Cancer Registry during 1973. The results obtained in a questionnaire survey (response rate, 75%; 54% of the total series) indicated that men lip cancer patients had engaged in outdoor work and smoking with significantly greater frequency than had the male controls. Together, these two risk factors posed a markedly increased risk (relative risk = 15.4). However, when the factors were analyzed separately, to exclude the effect of one on the other, no significant risk was noted. The frequency of recurrent herpetic infections was significantly greater in the men with lip cancer than in the men with head and neck cancer. No significant differences were apparent with respect to urban or rural residence. A negative geographic correlation exists between the amount of total solar radiation and lip cancer in Finland. Therefore, the main risk of lip cancer is probably the synergistic effect of another climatic factor and smoking. The risk associated with outdoor work (and perhaps also with herpetic ulcers) may lower the resistance of the vermillion border of the lip, thus increasing its susceptibility to tobacco carcinogens. (35 Refs)

10. RISK FACTORS OF LIP CANCER: A CRITICAL EVALUATION BASED ON EPIDEMIOLOGICAL COMPARISONS.

Lindqvist C
Finnish Cancer Registry, Liisankatu 21 B, 00170 Helsinki 17, Finland
Am J Public Health; 69(3):256-260 1979

The incidences of cancer of the lip, head and neck skin, and oral cavity in Finland during 1953 through 1973 were investigated. The mean annual number of new cases of lip cancer was 151 for men and 14 for women; the incidences of skin and intraoral cancers were lower, especially for men. The incidences of lip and skin cancers and, to a lesser extent, intraoral cancer decreased during the 1960's. The incidences of all three cancers increased with age, but unlike the other two, lip cancer showed a marked decrease in incidence in the oldest age groups. The risk of contracting lip cancer was higher in rural than urban areas and higher in the northern and eastern parts of the country than in the south. The risk of skin and intraoral cancers was higher in urban than rural areas. The incidence of lip cancer was negatively correlated with those of skin, colon, and prostate cancers and positively correlated with those of lung, laryngeal, and stomach cancers (the latter 2 in men only). The geographic correlation between the incidence of lip cancer in men and median income was negative, whereas that between the incidence of lip cancer in men and the proportion of those employed in agriculture was positive. The data suggest that lip cancer is etiologically related to upper gastrointestinal and respiratory tract cancers, but not to head and neck skin cancer. The strong positive association between lip and lung cancer suggests that tobacco smoking is a major common risk factor. (27 Refs)

11. ORAL AND PHARYNGEAL CANCER IN TEXTILE WORKERS.

Moss E
Dept. Occupational Health, Univ. Manchester, Manchester M13 9PT, England
Ann NY Acad Sci ; 271:301-307 1976

The association between oral and pharyngeal cancers and industrial exposure to textiles was studied in a morbidity survey of women in the northwest region of England, where textile processing is almost entirely of cotton. An association was found that could not be accounted for by wearing of dentures, by smoking and drinking habits, or by chewing. Although oral cancer is a rare disease, the textile industry is worldwide, and since much of the excess seems to be associated with processing of raw fiber, it is possible that the primary producers throughout the world, e.g., cotton ginners and sheep shearers, could also be at risk. (4 refs)

12. CANCER OF THE UPPER ALIMENTARY TRACT AND LARYNX IN POLAND AND IN POLISH-BORN AMERICANS.

Staszewski J
Inst. Oncol., Gliwice, Poland
Br J Cancer; 29(5):389-399 1974

Age-specific mortality rates for cancers of the buccal cavity, pharynx, esophagus, and larynx were computed for Poles between the years 1959 and 1972 and for Polish-born Americans in the periods 1950 and 1959-1961. The patterns of occurrence of these cancers in Poland appear to be similar to those of other European and American Countries, except perhaps for the rather high and still increasing incidence of laryngeal cancer. Among male Polish migrants, however, mortality for these cancers was distinctly higher than among native Poles or Americans. This contrast, which was largest for esophageal and laryngeal cancer, decreased between 1950 and 1959-61, but only among those aged below 65 years. The observed large shifts in the migrant's cancer risk suggest the operation of environmental rather than genetic factors. These shifts are similar to those seen in the incidence of lung cancer among Polish migrants to the U. S.

13. SMOKING HABITS AND DISEASE IN PENNSYLVANIA.

Hammond EC, Halloran JJ, Nicodemus EC
Statist. Res. Sec., Amer. Cancer Soc., New York, N. Y.
Pa Med; 67(10):19-23 1964

The findings of this first follow-up (34.5 mo) in Pennsylvania agree with those of the larger group of the 1959 prospective epidemiologic study of smoking habits, morbidity, and mortality rates as reported in CRA 2(7):#1368, 1964. This report covers 40,432 males aged 40-89 traced through 1962. Death rate from cancer of the lung was approx. 6 times as high among smokers of 40 or more cigarettes daily as among those who smoked 1-9 cigarettes daily. Of 74 lung cancer deaths in men between the ages of 40-89 yr, only 1 was a nonsmoker; the lung cancer rate was higher in those who began to smoke at an early age. Of 25 who died of cancer of the buccal cavity, pharynx, larynx, esophagus, and bladder, only 1 was a nonsmoker.

14. SMOKING HABITS AND HEALTH IN IOWA AND NEIGHBORING STATES.

Hammond EC, Stocks A
Statist. Res. Sec., Amer. Cancer Soc., New York, N. Y.
J Iowa Med Soc; 54(10):563-567 1964

In an epidemiological study in which cigarette smoking is indicated as a serious hazard to health, it is reported that of 204 men who died of lung cancer at the age of 40-89 yr, 9/204 had smoked cigars or pipes, while 188/204 had smoked cigarettes regularly. The lung cancer death rate of cigarette smokers increased markedly with the amount of smoking, and was 10x higher in cigarette smokers than in nonsmokers. Of 86 patients who died of cancer of the buccal cavity, pharynx, larynx, esophagus or bladder, 17/86 had smoked pipes or cigars, 22/86 cigarettes only. (See also CRA 2(2):#181; ibid; and ibid, (7):#1369 and #137C, 1964)

15. SMOKING AND CANCER. RETROSPECTIVE STUDIES AND EPIDEMIOLOGICAL EVALUATION.

Levin ML
Roswell Park Mem. Inst., Buffalo, N.Y.
J Chronic Dis; 16(5):375-381 1963

Among male patients seen at Roswell Park Memorial Institute from 1945-1956 the incidence (percentage) of various types of cancer seen among 7145 nonsmokers and 3016 cigarette smokers was, resp: lung, 6.8 and 66.8; larynx 7.5 and 61.0; lip 14.4 and 45.5; buccal cavity, 10.3 and 48.0; pharynx, 12.5 and 53.9; bladder, 17.3 and 52.1; esophagus, 16.9 and 48.7. Total incidence was 25.7% (controls) and 39.2% (cigarette smokers). The relative risks for developing lung cancer when figures were adjusted for age and residence by smoking status were for cigarette smokers, 5.04; other smokers, 1.39; and nonsmokers, 1.00. When data were collected from a retrospective hospital study, the relative risks of male cigarette smokers for developing lung cancer was 6.3; cancer of mouth-pharynx-esophagus, 2.55 and bladder, 1.99; when data were collected from a prospective study of mortality data the risks for these same sites were 9.85; 2.18; and 1.93, resp. There is no available evidence that some characteristic other than smoking is responsible for this increased disease risk.

16. SMOKING AND MORTALITY: A PROSPECTIVE STUDY.

Weir JM, Dunn JE
Dept. Public Health, Bureau Dental Health Education, American Dental Assoc., 211 East Chicago Ave., Chicago, IL
Cancer; 25(1):105-112 1970

The mortality experience of 68,153 men, 35 to 64 yr of age, over a period representing 482,658 person-yr of observation during which 4,706 known deaths occurred is related to their cigarette smoking habits. The findings are compared to the several other prospective studies reported in recent yr relating mortality to cigarette smoking. All studies are in essential agreement that cigarette smoking increases the risk for cancer of the mouth, larynx, esophagus, lung, kidney, and bladder. A few other tissue sites appear to carry increased risk of cancer as a result of cigarette smoking in one or another study but without unanimity. The risk gradient for lung cancer by age and amount of smoking increases in successive 10-yr age groups to be max at 55 to 64 yr in our study. Other diseases related to cigarette smoking in this and other prospective studies are gastric ulcer, emphysema, aneurysm, general arteriosclerosis, and arteriosclerotic heart disease. The latter is especially important because of the large number of deaths involved. The relative risk gradient for arteriosclerotic heart disease by age and amount of cigarette smoking was found to be max in the youngest age group comprising men 35 to 44 yr of age and lessens with increasing age. Future studies should be directed toward identifying other variables with which cigarette smoking interacts in those individuals developing disease. (Author abstract) (10 Refs)

17. DIFFERENCES OBSERVED IN THE SITE INCIDENCE OF CANCER, BETWEEN THE PARSI COMMUNITY AND THE TOTAL POPULATION OF GREATER BOMBAY: A CRITICAL APPRAISAL.

Jussawalla DJ, Deshpande VA, Haenszel W, Natekar MV
Indian Cancer Soc. Bombay Cancer Registry
Br J Cancer; 24(1):56-66 1970

The records of the Bombay Cancer Registry for 1964-1966 disclosed 9703 new cases of cancer, including 362 in the small Parsi community. Age-adjusted incidence rates/100,000 for all tumors combined and for several specific cancers were markedly different in the Parsis from the rates observed in Greater Bombay. Rates for cancer of the oral cavity, pharynx, larynx, esophagus and cervix were lower, and rates for cancer of the breast (female), uterus, prostate, ovary and skin and for all leukemias, were higher, in the Parsis than in the Bombay population. These differences were not removed by age-adjusting the data; the Parsis have an age structure very different from that of the general population, with a higher proportion of persons over 50 yr old. Some of the differences in relative cancer rates between the Parsis and the Bombay population are attributed to environmental factors, such as their high socioeconomic status and their sanctions against tobacco smoking.

18. A STUDY OF LUNG CANCER IN RELATION TO BIDI SMOKING IN DIFFERENT RELIGIOUS COMMUNITIES IN BOMBAY.

Notani PN, Rao DN, Sirsat MV, Sanghvi LD
Tata Memorial Center, Parel, Bombay-400 012, India
Indian J Cancer; 14(2):115-121 1977

A retrospective study was conducted of 683 male lung cancer patients and 1,279 male noncancer patients seen in one Indian hospital between 1963 and 1971 to examine geographic/religious differences in smoking habits in relation to lung cancer. Compared with nonsmokers, the estimate of relative risk for bidi smokers a relatively small cigarette containing only 0.25-0.50 g tobacco flakes wrapped in a piece of dried temburni (Diospyros melanoxylon) leaf and cigarette smokers was 3.38 and 2.36, respectively. Bidi smoking is much more prevalent in India and bidi smoke has a higher level of toxic agents and carcinogenic hydrocarbons than cigarette smoke, yet the overall incidence of lung cancer in India is much lower than that in Western countries. The coarse variety of bidi tobacco plus the uneven burning of the bidis may lead to an internal dispersal of smoke particles that would have greater impact on sites further up the respiratory tract, before the lungs are reached. The estimate of relative risk of bidi smokers for oropharyngeal cancer was 10.37, compared to those who neither smoke nor chew betel leaf, indicating that the max impact of bidi smoke is on the oropharynx. In every category of bidi smoking the Muslims had the highest relative risk, although they did not smoke more or for a longer duration than the Hindu smokers. These differences indicate the presence of other, as yet unidentified, modifying factors. (14 Refs)

19. A REPORT ON THE STUDY OF ORAL CANCER AND PRECANCEROUS LESIONS AMONGST 57,518 WORKERS OF GUJARAT. PHASE I.

Smith LW, Mani NJ, Bhargava K, Malaowalla AM
Oral Cancer Res. Project, Government Dental Coll. and Hosp., Ahmedabad 380016, Gujarat, India
A Report on the Study of Oral Cancer and Precancerous Lesions Amongst 57,518 Workers of Gujarat. Phase I. Gujarat, Government Dental College and Hospital, 174 pp., 1974.

A report is presented on the study of oral cancer and precancerous lesions in 57,518 industrial workers from Gujarat, India. Topics discussed include a review of the literature on the frequency and epidemiology of oral cancer in India, oral precancerous lesions, and the role of Indian oral habits such as smoking, tobacco chewing, and snuff inhalation. Epidemiological aspects discussed include oral habits, religion, and education. The results of clinical examinations, location of lesions, lymph node involvement, presence of pain, and trauma are presented. Cytological and histological data are discussed.

B. Selected Clinical Observations Concerning Etiological Factors in Tobacco-Related Oral Cancer

20. OBSERVATIONS ON THE EFFECTS OF TOBACCO SMOKE ON THE ORAL MUCOSA.

Borota A, Morse JL, Owrandi M
Dept. Derm., N.Y. Med. Coll., New York
J Am Geriatr Soc; 12(1):67-70 1964

In a 4-part study, examination of the oral cavity of 1,529 geriatric patients, 9 cases of oral mucosal cancer were found among 1,006 smokers while only 1 case was seen among the 523 nonsmokers. These patients represented a fairly homogeneous group with similar backgrounds and identical nutritional factors, and were available for follow-up. In part 4 of the study (examination of 750 patients) 4 smokers with squamous cell cancer all smoked cigarettes and showed leukoplakia; 2 were in what are judged potentially dangerous occupations (carpenter and artist, painter).

21. PRECANCEROUS LESIONS OF THE ORAL CAVITY.

Bianchi HB
Paraguay 4092, Buenos Aires
Hospital (Rio De J); 63(4):767-781 1963

On analysis of 320 cases of leukoplakia observed between 1937 and 1956, 40% were among tobacco users, 10% could be attributed to prolonged local irritants, 8% were associated with syphilitic lesions, and the remainder were idiopathic. In a smaller series of 98 patients, age distribution for 58 males and

40 females was, resp: 20-30 yr, 4 and 2; 30-40 yr, 6 and 8; 40-50 yr, 16 and 10; 50-60 yr, 15 and 12; 60-70 yr, 17 and 8. No lesions were seen in patients younger than 20 yr. In most patients, the lesions remain stationary for up to 10 yr; but in a few patients over 40-50 yr of age, the plaque may acquire a reddish color and (eventually) a verrucose surface. These Grade IV lesions may eventually ulcerate, become indurated, and be accompanied by local adenopathy. These cancers should be differentiated from the carcinomas in situ found on biopsy of some leukoplasias. Differential diagnosis and treatment of precancerous leukoplakias are reviewed briefly.

22. PRECANCEROUS LESIONS OF THE MOUTH.

Kramer IR
Dept. Pathology, Inst. Dental Surgery, Eastman Dental Hosp., Gray's Inn Road, London, WC1X 8LD, England
J Laryngol Otol; 90(1):95-100 1976

A condition is termed precancerous if the risk of malignant change is sufficiently high to influence the management. Several precancerous lesions of the mouth are described. White sponge nevus shows as thickened epithelium with an irregular surface; characteristic changes occur in the superficial part of the prickle cell layer. The cells have a vacuolated appearance, with most of the cytoplasm seemingly pushed out to the periphery; it is believed that white sponge nevus is harmless. Floor-of-the-mouth keratosis presents as a soft white patch; biopsy shows an atrophic epithelium with a well-defined keratinized layer. This condition is considered dangerous. Another condition, lichen planus, varies considerably in appearance; one common feature is the presence of tiny whitish spots. Often the developed form appears as a network of slightly raised grey-white lines set on a mucosa that does not appear inflamed. Carcinoma may arise in lichen planus, but probably such changes are rare. Candida albicans, found in about 50% of normal mouths, may invade the superficial layers of the epithelium to produce a chronic hyperplastic infection. Biopsy shows that the epithelium is parakeratinized and the hyperplasia may be gross. Some evidence suggests that chronic candidal infection significantly predisposes to carcinoma. One common cause of the conditions of leukoplakia and erythroplakia is smoking; there is also idiopathic leukoplakia, which varies greatly in appearance. Evidence suggests that the risk of carcinoma may be greater in idiopathic than in smoker's leukoplakia. Erythroplakia, however, should be regarded as carcinoma until proved otherwise. Speckled leukoplakia, as well as any leukoplakia with reddened areas, should be suspected of malignancy. It is suggested that a computer could be valuable in the diagnosis of suspect lesions. Many mouth cancers were preceded by recognizable precancerous lesions; better recognition of these lesions is recommended. (29 refs)

23. SMOKING HABITS AND HISTOLOGICAL CHARACTERISTICS OF ORAL LEUKOPLAKIAS IN DENMARK AND HUNGARY.

Roed-Petersen B, Banoczy J, Pindborg JJ
U. Hosp., Copenhagen, Denmark
Br J Cancer; 28(6):575-579 1973

The histological characteristics of oral leukoplakia were studied in relation to the smoking habits of 345 Danish and 184 Hungarian leukoplakia patients. No significant relationship between smoking habits and keratinization, epithelial thickness, epithelial dysplasia, or inflammation was found. However, nonsmokers were more likely to show hyperorthokeratosis, while smokers were more likely to show hyperparakeratosis. Similarly, the smokers showed a higher frequency of moderate to severe inflammation as compared with the nonsmokers.

24. INCIDENCE OF ORAL LEUCOPLAKIAS AMONG 20,358 INDIAN VILLAGERS IN A 7-YEAR PERIOD.

Mehta FS, Pindborg JJ, Bhonsle RB, Sinor PN
Basic Dental Research Unit, Tata Institute of Fundamental Research, Bombay, India
Br J Cancer; 33(5):549-560 1976

A group of 20,358 villagers in two districts of India has been followed for 7 years to study the incidence of oral leucoplakia. The follow-up rate of the population in the two districts ranged from 61% to 71%. In one of the districts (Bhavnagar) no new cases of leucoplakia were found among females in the 7-year period. Among males 105 cases developed (4.0/1000/year). The incidence was highest among hookli (clay pipe) smokers. In the Ernakulam district the incidence among males was 3.3/1000/year whereas among females it was 1.9/1000/year. The mixed habits group had the highest incidence of oral leucoplakias (7.2 and 9.9/1000/year among males and females respectively). (Author Abstract)

25. THE NATURAL HISTORY OF ORAL LEUKOPLAKIA. (PP. 83-91)

Mehta FS, Hamner JE, Pindborg JJ
Basic Dental Res. Unit, Tata Inst. Fundamental Res., Homi Bhabha Road, Bombay 400 005, India
Prevention and Detection of Cancer. Part II. Detection. Vol. 1. High Risk Markers. Detection Methods and Management. Nieburgs HE, ed.New York, Marcel Dekker, 1299 pp., 1978.

The natural histories of oral leukoplakia (LP), other possible oral precancerous lesions, and oral cancer were studied in an epidemiologic survey of 50,915 adults in India. The incidence rate for LP was 2.1/1,000 men and 1.6/1,000 women, the peak incidence rate being in the age group 55-64 yr among men and in the age group 45-54 yr among women. The incidence was zero among individuals who did not use tobacco and was highest (5.3/1,000) among those who both chewed 'pan' (a combination of betel leaf, lime, areca nut, and tobacco) and smoked 'bidi' (coarse tobacco rolled in a dry temburni leaf). Among tobacco users, bidi smokers exhibited the lowest incidence rate (1.0/1,000). Ten oral cancers (squamous cell carcinoma) were detected among individuals with LP, four were found among those with no oral lesions. The rate of malignant transformation of LP was zero among those aged less than 35 yr, 5.5/1,000 among those aged 35-54 yr, and 13.7/1,000 among those aged greater than or equal to 55 yr. The rate of malignant transformation was twice as high for women (11.1/1,000) as for men (5.1/1,000) and twice as high for tobacco chewers (11.5/1,000) as for those who chewed and smoked (6.4/1,000). Malignant transformation was not observed among those who only smoked. The data suggest that LP's associated with different tobacco habits may have different natural histories. (5 Refs)

26. ANATOMICOCLINICAL AND HISTOPATHOLOGIC STUDY OF ORAL KERATOSES.

Garay JC
Departmento de Patologia de la Escuela de Estomatologia de la Universidad de La Habana, Havana, Cuba
Rev Cubana Estomatol; 13(2):135-145 1976

The clinical and histopathologic aspects of 112 patients with oral keratotic lesions are reviewed. The lesions were found mainly in white men who smoked and were most frequently seen in the lower lip and the cheek mucosa. According to the histopathologic classification, 2 diffuse dermatoses, 40 focal dermatoses, 59 leukoplakias, and 11 epidermoid carcinomata were found. The significance of the histopathologic examination is stressed, not only for the identification of leukoplakias by dyskeratoses but also for diagnosing carcinomata that initially appear as dermatotoic patches. The literature is reviewed. (46 Refs)

27. SUBLINGUAL KERATOSIS AND MALIGNANT TRANSFORMATION.

Pogrel MA
H. M. Stanley Hosp., St. Asaph, Wales
J Oral Pathol; 8(3):176-178 1979

The rate of malignant transformation in 19 patients with sublingual keratosis (SK) was studied. Carcinoma subsequently developed in three patients. The SK patients ranged in age from 48-73 yr and included 12 women and 7 men. Among the patients who developed carcinoma there were two men aged 48 and 61 yr and a 65-yr-old woman. The carcinomas developed 4-7 yr after SK. Eight SK patients were heavy smokers, and carcinoma developed in two of them. A fourth SK patient developed carcinoma of the lateral border of the tongue 5 yr later in an area unaffected by leukoplakia. Of the 16 patients who showed no malignant transformation of leukoplakia, 3 remained unchanged, three had repeated biopsies taken, 4 improved, and 6 could not be evaluated on the basis of available information. In a series of 23 patients with carcinomas of the floor of the mouth, the carcinoma arose in a preexisting white lesion in 8 cases. The results suggest that SK has a considerable risk of malignant transformation and that biopsy and meticulous follow-up are mandatory. (5 Refs)

28. EXPERIENCE WITH CARCINOMAS OF THE DIAPHRAGMA ORIS.

Douniau R
No affiliation given
Ann Otolaryngol Chir Cervicofac ; 93(3):232 1976

Twenty five epitheliomas of the diaphragma oris and 25 epitheliomas of the tongue were reviewed in terms of etiology (age, sex, tobacco use, precancerous lesions), classification of the tumor, history, treatment, and prognosis. Results were discouraging. (no refs)

29. BUCCAL FLORID PAPILLOMATOSIS OR VERRUCOUS CARCINOMA.

Grinspan D
Departamento Dermatologia, Facultad de Ciencias
Medicas, Universidad Buenos Aires, Buenos Aires, Argentina
Acta Odontol Venez; 16(1):21-38 1978

Experience is presented on 79 cases of buccal florid papillomatosis (PF) seen since 1975. Most cases occur between the ages 40-70 yr, with the highest incidence between ages 55-65. Male to female sex ratio is approx 10:1; occurrence is chiefly in the white race. Lesions may be single or multiple and may develop on healthy mucosa or other lesions (leukoplakia, lichen, chronic lupus erythematosus, cheilitis, candidiasis). The lesions present as vegetations, at times verrucous in appearance with a damp surface. Fistulas to the skin may develop, giving rise to maxillary necrosis. Four histologic types are described which do not necessarily constitute evolutionary stages. Type IV represents classical carcinoma but with characteristics of the other types of PF. While no metastases occur in Type IV cases, about 10% show transformation to classical spinocellular epithelioma, especially in those who have had radiotherapy. FP is considered to be a cancer with a low potential for malignancy. Many of the patients smoke or chew tobacco, betel or use snuff. Systemic or regional ia treatment with methotrexate generally does not produce complete cures but reduces the size of the lesions after which surgery, cryosurgery or electrocoagulation may be instituted. Radium therapy has been found very efficient. Cures are achieved in 75% of the cases. (11 Refs)

30. A REPORT ON THE STUDY OF ORAL CANCER AND PRECANCEROUS LESIONS AMONGST 57,518 WORKERS OF GUJARAT. PHASE II.

Malaowalla AM, Mani MJ, Bhargava K, Smith LW, Silverman S, Bilimoria KF
Oral Cancer Res. Project, Government Dental Coll. and Hosp., Ahmedabad 380016, Gujarat, India
A Report on the Study of Oral Cancer and Precancerous Lesions Amongst 57,518 Workers of Gujarat. Phase II. Gujarat, Government Dental College and Hospital, 164 pp., 1974.

Phase II of a report on the study of oral cancer and precancerous lesions in 43,654 textile mill employees of the city of Ahmedabad and nearby places, such as Kalol, Nadiad, and Baroda in Gujarat, India is presented. Topics discussed include the fate of lesions during a 2-yr period. Clinical, cytological, and histopathological aspects of these lesions, which include leukoplakia, submucous fibrosis, nicotine stomatitis, and lichen planus, are discussed. The incidence, location, cytology, histopathology, and relative and attributable risks of newly developed lesions are presented and discussed.

31. ORAL CYTOLOGIC PATTERNS IN RELATION TO SMOKING HABITS. SOME EPITHELIAL, MICROFLORAL, AND LEUKOCYTIC CHARACTERISTICS.

Hillman RW, Kissin B
125 Locust St., Garden City, NY 11530
Oral Surg Oral Med Oral Pathol; 42(3):366-374 1976

Papanicolaou smears of cheek and tongue scrapings taken from 790 alcoholics (99% men: 52% 50 yr old) were studied cytologically to see if there was a relation between cell characteristics and cigarette smoking. Preparations from smokers generally showed a greater nucleus and cell size, a greater frequency of both cornified and late cornified cells, and smaller concentrations of bacteria, fungi, and filamentous forms and, probably, WBC. A dose-related frequency was indicated. These findings correlate with the view that microscopic changes are frequent in clinically unremarkable areas of the mouth and that tobacco induces some of the cellular changes to which its use has been clinically and epidemiologically oriented. (42 Refs)

32. SMOKING AND MOUTH-THROAT CANCER.

Moore C
Dept. Surg., U. Louisville Sch. Med., Ky.
Am J Surg; 108(4):565-569 1964

A 6.8-yr follow-up study is presented of 78 men and women (male:female ratio 2.5:1) with squamous carcinoma of the mouth or throat whose av age was 57.6 yr and who were living and well more than 3 yr after treatment of the disease. Prior to the study, 66/78 had smoked more than 1 pack of cigarettes daily for an av of 36.4 yr, while the remainder used various forms of tobacco (pipe, cigar, chewing tobacco, snuff, cigarettes and various combinations thereof) during the same over-all period. Among 29 who quit smoking after treatment, only 1 developed a second squamous carcinoma. Among 49 who continued smoking, 17 developed second cancers after an av of 5.7 yr. This significant difference in incidences of second cancers is believed to support a causal relationship between tobacco and mouth-throat cancer.

33. MULTIPLE MALIGNANT PRIMARY TUMORS OF THE ORAL CAVITY AND THE UPPER RESPIRATORY TRACT.

Kuhn E
Cancer Radiol. Inst., Gen. Hosp., Budapest, Hungary
Z Laryngol Rhinol Otol; 42(7):521-528 1963

During a period of 14 yr, among those treated, a total of 36 patients (30 male, 6 female, age 42-79 yr) had multiple malignant primary tumors of the oral cavity and the upper respiratory tract. Histologically the tumors were squamous cell carcinomas; they were synchronous (within 6 mo) in 12/36 (33.3%), and metachronous in 24. Family history was positive in 30, among whom 8 had cancer; 85% of the patients were smokers. Among 33 patients studied, leukoplakia was present in 21 and was most severe in those cases with more than 2 tumors; 9/36 had a history of syphilis and 6/9 exhibited syphilitic leukokeratosis. Among the metachronous cases, the intervals varied from 1 to 27 yr. In cases where the precancerous changes were severe, the latent period for the second tumor was briefer.

34. DOUBLE AND SECOND PRIMARY CARCINOMAS IN THE BUCCAL CAVITY.

Koch H
Dusseldorf, W. Germany
Fortschr Kiefer Gesichtschir ; 21:185-187 1976

A review is presented of 10 patients, (7 men, 3 women; av age 62.5 and 55.6 yr, respectively) with double carcinoma, and 13 patients (8 men, 5 women, av age 58.7 yr) with successive or multiply occuring carcinomas (SC). In the former group, hepatitis or cirrhosis occurred in three, hyperthyroidism in one and diabetes in one; four patients were alcoholics or heavy smokers. The cheek was involved in four patients, the mandibular alveolar process and buccal mucosa in one, the buccal palate in one, the mandibular lip in one, the mandibular lingua in one, the mandibular palate in one, and there was bilateral mandibular involvement in one. Resection was performed in nine patients; one received radiation therapy. Five patients have survived 5 yr and three have remained recurrence-free for 1 to 2 yr. In the SC patients, five had hepatobiliary or gastrointestinal disease and five were heavy smokers. The regional distribution was as follows: one palatal-cheek, two cheek-lip, two mandibular-palatal, two mandibular-lingual, two mandibular-maxillary, one mandibular-lip, and one buccal-palatal. The first tumors were precanine or anterior postcanine; the second tumors were usually posterior canine. All were treated surgically; four are tumor-free for 5 yr. The TNM stages of the patients of both groups are presented. (16 refs)

35. SEPARATE PRIMARY CARCINOMAS OF THE ESOPHAGUS AND HEAD AND NECK REGION IN THE SAME PATIENT.

Cahan WG, Castro EL, Rosen PP, Strong EW
Memorial Sloan-Kettering Cancer Center, 1275 York Avenue,New York, NY 10021
Cancer Suppl; 37(1):85-89 1976

From 1949 to 1972 at Memorial Sloan-Kettering Cancer Center, 60 patients with primary cancers of both the oral cavity, pharynx, larynx (OPL) and esophagus were studied. In 15, the cancers occurred synchronously, and in 68% they occurred within 2 years of each other, the longest interval being 27 years. The tongue and extrinsic larynx were the most common sites or origin together with the middle third of the esophagus. During the same period, over 7000 patients with OPL and over 1000 patients with esophageal cancer were seen at this institution. The majority of patients had a history of excessive smoking and alcohol intake. Four out of nine who had previous radiation therapy for their OPL cancer developed esophageal cancer within the therapeutic field (three after 16, 25, and 27 years). Thirty percent (18/60) had three primary cancers; one had four, of which two were in the head and neck region. Two patients survived more than 5 years; both also had a third primary cancer of the lung. There are broader implications in this study: multiple primary cancers in general, and this group in particular, give us especially valuable clues as to the oncogenic influence of environmental factors as well as cellular, organ, and also systemic susceptibility. With one cancer, one can anticipate formation in other related organs. This provides an opportunity for early diagnosis, more effective management, and improved survival. The cause and effect relationship of tobacco and alcohol must be emphasized at every opportunity and most particularly to those who have developed one cancer in the oropharyngeal-laryngeal region.

36. EPIDEMIOLOGIC INVESTIGATION OF MULTIPLE PRIMARY CANCER OF THE UPPER ALIMENTARY AND RESPIRATORY TRACTS. I. A RETROSPECTIVE STUDY.

Wynder EL, Dodo H, Bloch DA, Gantt RC, Moore OS
Sloan-Kettering Inst. Cancer Res. New York, N. Y.
Cancer; 24(4):730-739 1969

A retrospective study was made of 104 patients with multiple primary cancers of the mouth, pharynx and larynx. The women developed their first and second primary tumors at a slightly younger age than men and the interval between diagnosis of the 2 primaries ranged from 8 mo to 30 yr, 9 mo in women and 2 mo to 26 yr, 11 mo in men. Both tumors arose in the same anatomic region in 26% of the men and 19% of the women. Most commonly, the first primary occurred in the anterior two-thirds of the tongue or the intrinsic larynx in men and the anterior two-thirds of the tongue and the floor of the mouth in women. In comparison with a control group of 776 male single primary patients, 97% of the double primary patients and 87% of the single primary patients smoked more than 20 cigarettes a day preceding diagnosis. There were no nonsmokers in the former group and only 3% nonsmokers in the single primary group. In the former group, 53% smoked more than 2 packs a day compared with 43% of single primary patients. The double primary patient who smoked 2 packs a day before initial diagnosis, developed second primaries within 9 yr. Among the women who developed a second primary within 9 yr, 22% smoked more than 2 packs a day compared with 13% of 249 single primary controls. In a comparison of smoking habits after diagnosis of the first primary, 55% of the men and 63% of women who developed a second primary and 28% of the men and 25% of the women in the single primary group continued to smoke. There was also a significantly higher frequency of radiation therapy in male patients who developed second primaries 10 or more yr after the first. Continued alcohol consumption had no significant effect on the occurrence of a second primary tumor.

37. MULTICENTRIC METACHRONOUS PRIMARY CARCINOMA OF THE UPPER ALIMENTARY TRACT IN 'BIRI' SMOKERS.

Gill RS, Gill JK, Rhotgi VK, Mishra UC, Lal M
Dept. ENT, S. N. Medical Coll., Agra, India
J Laryngol Otol; 93(5):527-531 1979

The occurrence of multiple metachronous primary squamous cell carcinomas of the upper alimentary tract in three Biri smokers (a form of cheap cigarette made by rolling sun-dried, uncured tobacco in dried leaf of Tamburni) smokers is reported. A 45-yr-old man with a long history of heavy (40-50/day) Biri smoking presented with a squamous cell carcinoma of the left pyriform fossa. After radiotherapy, he reduced the number of Biris smoked/day by half, but he presented 13 yr later with a SCC of the left tonsil. A 50-yr-old Biri smoker (30-50/day) presented with a SCC of the left cheek. He was treated with surgery and radiotherapy, and he reduced his smoking to approx 16/day. After 4 yr and 10 mo later, he presented with a SCC of the soft and hard palates. A 40-yr-old man who smoked 20-30 Biris/day presented with a SCC of the left pyriform fossa. He was treated with radiotherapy, but returned 2.5 yr later with a SCC of the esophagus. In all three cases, the second tumors responded to radiotherapy. (10 Refs)

38. ORAL CARCINOMA: ANALYSIS OF ONE HUNDRED AND EIGHTY-NINE CASES.

Gardner AF, Hamburger S, Love S
Dept. Path., Baltimore Coll. Dent. Surg., Maryland
J Am Dent Assoc; 66(4):456-465 1963

A survey of the incidence, history and clinical and histological features in 189 patients (184 males and 5 females) with intraoral carcinoma (tongue, buccal floor, lips, tonsillar region, buccal mucosa, etc in that order) treated by the USPHS in Baltimore between 1941 and 1960 showed that oral cancer is primarily a disease of the aging white male, the group having mean age of 56.5 yr and including only 15 non-Caucasians; 91% of the lesions were squamous cell carcinoma. Most of the patients had been seamen, 94.2% used tobacco and/or alcohol (49.7% were heavy smokers), 43.4% were edentulous, 36% wore dental prostheses and more than 50 patients showed poor oral hygiene. The case histories revealed a possible association between oral cancer and syphilis, diabetes mellitus, senile epithelial changes, tuberculosis, nutritional deficiencies and cardiovascular disease. Local irritation seems to be an important factor in the etiology, and an inherited predisposition is suggested.

39. CANCERS OF THE MOUTH.

Jaumet E, Maisin J, Deckers C
Cancer Inst., U. Louvain, Belgium
J Radiol Electrol Med Nucl; 44(11):727-734 1963

In a review of the etiology, symptomatology, classification and treatment of oral cancers (excluding cancers of the tongue), the authors present an analysis of 148/155 original cases seen at a mean age of 61.74 yr (range, 28-82 yr) for men and 64.5 yr for women. Males comprised 84% of the pt group. All cases seen involved spinocellular or epidermoid carcinomas (although the authors report having also seen pts with epulis, mixed tumors, myeloplax, plasmacytomas, cylindromas, and spindle sarcomas). A majority of these pts were or had been smokers. Stumps of teeth or poorly fitting dentures, which provoked chronic mucosal irritation, were frequently seen. One cancer was developed from a syphilitic lesion; positive Bordet-Wassermanns were obtained in 3/18 pts tested. In 8/27 female pts included in fragmentary study, cancers developed from leukoplakia. The authors report that oropharyngeal cancers account for 1-1% of all reported neoplasms in Belgium.

40. CHRONIC MECHANICAL TRAUMA IN THE AETIOLOGY OF ORO-PHARYNGEAL CARCINOMA.

Thumfart W, Weidenbecher M, Waller G, Pesch HJ
Universitats-HNO-Klinik, Waldstrasse 1, D-8520
Erlangen, W. Germany
J Maxillofac Surg; 6(3):217-221 1978

The etiology of oropharyngeal carcinoma was studied in 86 patients with tumors of the oral cavity. Tumors of the gum and palate accounted for 62% of these tumors. Most (83%) of the patients were smokers and 49% regularly consumed alcohol, some to excess. In 44% of these patients, there was a coincidence of the cancer site with the site of persistent mechanical irritation by sharp teeth edges, prominent parts of an ill-fitting denture, or similar mechanical factors. Most of the tumors were keratinizing, poorly differentiated, squamous cell carcinomas, and all carcinomas in contact with a mechanical irritation had a surrounding wall of chronic inflammatory infiltration. Dysplasias of different degrees were found in the areas around the carcinomas. (16 Refs)

41. MOUTHWASH AND ORAL CANCER: CARCINOGEN OR COINCIDENCE?

Weaver A, Fleming SM, Smith DB
Dept. Surgery, Wayne State Univ., Detroit, MI
J Oral Surg; 37(4):250-253 1979

Two hundred patients with squamous cell cancer of the head and neck were compared with patients from a general surgery group on the use of tobacco, alcoholic beverages, and mouthwash. Patients with cancer of the head or neck used significantly greater quantities of tobacco and alcoholic beverages than the control group. Ten of the 11 nonsmoking and nondrinking patients had used mouthwash at least twice daily for greater than 20 yr. Only two patients diluted the mouthwash, and nine used a brand containing 25% alcohol. Another six patients used alcoholic beverages and/or tobacco only occasionally, but all used mouthwash excessively. Two case histories are presented, both of which implicate mouthwash as a possible etiological agent in persons susceptible to squamous cell cancer. It is suggested that a history of mouthwash use be determined for all patients with premalignant or malignant lesions of the oral cavity to ascertain whether the use of mouthwash is coincidental to the development of oral cancer or is carcinogenic. (8 Refs)

42. SQUAMOUS CELL CARCINOMA OF THE ORAL TONGUE IN PATIENTS LESS THAN THIRTY YEARS OF AGE.

Byers RM
Head Neck Serv., Dept. Surg., Univ. Texas Syst. Cancer Cent., M. D. Anderson Hosp., Houston, Tex.
Am J Surg; 130(4):475-478 1975

In a series of 11 patients under age 30 with squamous cell carcinoma of the tongue, overall survival was lower than in older patients (45% versus 65% resp) and was not as clearly related to smoking, drinking or dental problems. Histological classification of Grade III (48% of cases) was prognostically unfavorable. The primary tongue lesion was well controlled by surgery in 2 cases, by irradiation (6,000 rads over a 6 wk period, followed by radium implant at the primary site) in 5 patients, radium implant alone in 1 patient, and combined surgery and irradiation in 3 patients; recurrences occurred in 6 patients, 4 of whom have since died. Treatment choice could be calibrated to TNM staging classification. (7 refs)

43. DNA-DEPENDENT DYE BINDING BY ORAL EPITHELIUM: ITS RELATION TO SMOKING HABITS.

Roth D, Oppenheim A, Fredrickson DT
New York U. Med. Ctr., N.Y.
Arch Environ Health; 17(1):59-61 1968

Quantitative changes in acriflavine binding (in proportion to cellular DNA content) were studied in oral epithelial samples from 807 subjects, mostly men. In samples from 350 nonsmokers, the mean binding rate (in 10-6 microg/cell) was 1.72; binding levels above 2.3 (the minimum seen in oral or upper respiratory cancer) were seen in 3.7% of the group (13/350). The dye uptake values in samples from 100 cigar smokers were not significantly different from control values. In samples from 257 cigarette smokers, mean values were 1.79-2.02 (above 2.3 in 56/257); a significant increase was seen in heavy smokers. A significant increase in dye binding was also noted in pipe smokers (mean 1.86; above 2.3 in 6/100 samples) and in subjects smoking cigarettes, pipes and cigars (mean 1.74; above 2.3 in 3/40 samples). In a small group of subjects who stopped smoking, dye binding values fell to normal after 6 mo of abstinence.

C. Alcohol, Diet and Smoking as Cofactors in Oral Cancer

44. A CASE-CONTROL INVESTIGATION OF ALCOHOL, TOBACCO, AND DIET IN HEAD AND NECK CANCER.

Feldman JG, Hazan M, Nagarajan M, Kissin B
Environmental Medicine and Community Health, State Univ. of New York, Brooklyn, NY, 11203
Prev Med; 4(4):444-463 1975

A comparative study of 150 patients with head and neck cancer (HNC), chiefly of the mouth, pharynx and larynx and a control group of 319 comparable patients with 'other' types of cancer from five New York City hospitals was carried out in order to investigate the relationship between alcohol, tobacco, and dietary intake before and after the diagnosis of cancer. This was of interest as both alcohol and tobacco consumption are related to HNC, and a better understanding of their role could result in suggestions for modifications of their intake. Male HNC patients were found not significantly different from the 'other' (control) male cancer patients in age, race, or socioeconomic status. The small number of female HNC patients differed from their controls, however; minimal emphasis was placed on their data, therefore statistically significant positive associations between alcohol consumption and HNC and between tobacco consumption and these cancers were demonstrated. The meaning of these associations was not clear, as most heavy drinkers are also heavy smokers. Data were combined with other data from the literature, regrouped, and analyzed statistically in order to evaluate the role of smoking and drinking in the etiology of HNC more specifically. The data suggested that smoking alone or in combination with light drinking is associated with a moderately increased risk to HNC; drinking by itself apparently does not substantially increase the risk. Heavy drinking accompanied by either light or heavy smoking is associated with a marked increase of HNC, and is greater in persons who both drink and smoke heavily. (17 Refs)

45. DENTITION, DIET, TOBACCO, AND ALCOHOL IN THE EPIDEMIOLOGY OF ORAL CANCER.

Graham S, Dayal H, Rohrer T, Swanson M, Sultz H, Shedd D, Fischman S
Dept. Social and Preventive Medicine, State Univ. New York at Buffalo, Buffalo, NY 14214
J Natl Cancer Inst; 59(6):1611-1618 1977

The role of dentition, diet, tobacco, and alcohol in the epidemiology of oral cancer was investigated in 584 men with histologically confirmed oral cavity cancers and 1,222 control men with nonneoplastic diseases. The risk of cancer increased from unity for patients who never smoked to 5.64 in those who were heavy smokers. Similar risks were observed for alcohol consumption: from unity at less than 1 drink/wk to 2.66 for greater than or equal to 14 drinks/wk. Evaluation of risk with respect to dentition indicated a risk of unity with adequate posterior and anterior dentition; this risk increased to 4.62 for inadequate total dentition. These risk factors appeared to be synergistic. The highest risk was observed for heavy smokers and drinkers with poor dentition (7.68). (18 Refs)

46. GEOGRAPHIC CORRELATIONS BETWEEN CANCER MORTALITY RATES AND ALCOHOL-TOBACCO CONSUMPTION IN THE UNITED STATES.

Breslow NE, Enstrom JE
Sch. Public Health, U. California, Los Angeles
J Natl Cancer Inst; 53(3):631-639 1974

Average annual age-adjusted cancer mortality rates for 1950-1967 were correlated with per-capita consumption of cigarettes, spirits, wine, and beer as estimated from tax receipts in 41 states of the United States in 1960. These correlations were made for cancers of 19 sites for white males and of 20 sites for white females. Multiple regression analyses were used to estimate the simultaneous effects on cancer mortality of state-to-state variation in the urban component of the population and in the consumption of spirits, beer, and cigarettes. Respiratory cancers were related to cigarette consumption, certain cancers of the upper alimentary tract to consumption of spirits, and cancers of the stomach, large bowel, kidney, bladder (for men), and breast (for women) to consumption of beer. The strongest single association was between rectal cancer and beer consumption, a result found also with similar data for 24 other countries. The hazards of attempting to draw sound scientific inferences from such data are acknowledged and must await confirmation and explanation by direct observation of the individual.

47. THE RELATIONSHIP OF THE USE OF TOBACCO AND ALCOHOL TO CANCER OF THE ORAL CAVITY, PHARYNX OR LARYNX.

Vincent RG, Marchetta F
Roswell Park Mem. Inst., Buffalo, N.Y.
Am J Surg; 106(3):501-505 1963

When 106 patients with carcinoma of the oral cavity, pharynx or larynx were interviewed, a history of heavy consumption of alcohol was given by 62% of the patients, and 85% smoked the equivalent of one or more packs of cigarettes a day. The male:female ratio was 5.2:1; mean age of diagnosis for the entire series was 62 yr. Of all the patients with oral carcinoma in this study, a second primary malignant lesion developed in 7.5%. Although the etiologic mechanism is not understood, additional supporting evidence indicates that the habitual use of tobacco and alcohol plays an important role in the cause of oral carcinoma.

48. THE ROLE OF ALCOHOL AND TOBACCO IN MULTIPLE PRIMARY CANCERS OF THE UPPER DIGESTIVE SYSTEM, LARYNX AND LUNG: A PROSPECTIVE STUDY.

Schottenfeld D, Gantt RC, Wynder EL
Memorial Hosp. for Cancer and Allied Diseases. New York, NY, 10021
Prev Med; 3:277-293 1974

A prospective study of 733 patients with a single primary epidermoid carcinoma of the oral cavity, pharynx, or larynx (OPL) first diagnosed at the Memorial Sloan-Kettering Cancer Center between 1965 and 1968 is presented. Fifty-three patients developed a new primary cancer of the upper digestive system, larynx, or lung by January, 1972; the av annual incidence in women was 15.4/1,000 and in men 18.2/1,000. The women in this study had consumed less alcohol and tobacco prior to the diagnosis of cancer than the men. At 5 yr, 433 deaths had occurred; 66.7% were due to metastases or complications of treatment of OPL cancer, 1.5% to a new primary cancer of the lung or esophagus, and 1.4% to a new non-respiratory or non-upper digestive tract cancer. Significant excesses in cancer mortality in both sexes existed in patients between 45 and 64 yr old; this was true at all levels of alcohol and tobacco consumption. The results of the study demonstrated that patients with greater than 30 yr of exposure to higher levels of tobacco and alcohol combined had about 4 x the risk of developing secondary primary epidermoid carcinomas of the upper digestive system, larynx and lung within 5 yr of diagnosis of the index cancer. It appears that, within the first 5 yr after diagnosis of the index cancer, altered smoking and drinking habits had no effect on the development of any new neoplastic process already initiated in exposed tissues. (18 Refs)

49. TOBACCO AND ALCOHOL CONSUMPTION IN RELATION TO THE DEVELOPMENT OF MULTIPLE PRIMARY CANCERS.

Wynder EL, Mushinski MH, Spivak JC
American Health Foundation, 1370 Ave. of the Americas, New York, NY 10019
Cancer Suppl; 40(4):1872-1878 1977

The relationship between tobacco use and alcohol consumption and the development of additional primary cancers of the upper alimentary tract is reviewed. The chance of developing a second primary depends principally on the intensity (ie, quantity and duration) of the smoking and drinking habit prior to the onset of the first neoplasm. However, results conflict regarding the effect exerted by the continuation of these habits after the first diagnosis. Although smoking is the primary risk factor associated with cancers in this area, its interaction with alcohol creates a powerful carcinogenic effect. It is agreed that multiple primaries are selective on a site-specific basis and that risk varies with anatomic location of the first primary. (20 Refs)

50. HEAVY DRINKING, SMOKING LINKED WITH ORAL CANCER.

Anonymous
No affiliation given
JAMA; 236(5):435 1976

A recent study of women who smoke and drink heavily indicated that exposure to both alcohol and tobacco can lead to the onset of oral cancer 15 yr or more earlier than usual in women who abstain from both. It is estimated that women between the ages of 40 and 64 yr who smoke and drink more than 30 ml of alcohol a day are at 18 times greater risk of mouth or tongue cancer than women who do not smoke and drink. Nicotine does not cause skin tumors in mice when applied directly to the skin, but acts more like a cocarcinogen. (no refs)

51. EARLY ONSET OF ORAL CANCER AMONG WOMEN WHO DRINK AND SMOKE.

Bross ID
Roswell Park Memorial Inst., Dept. Biostatistics, 666 Elm St., Buffalo, NY 14263
Oncology; 33(3):136-139 1976

Data from 145 white women with intraoral cancer and 1,973 nonneoplastic controls were examined to determine the effect of drinking and smoking on the age of cancer onset. Most of the women smoked a pack of cigarettes a day or less. Light drinkers were defined as those who drank less than 30 bottles of beer/mo, 30 glasses of wine/mo, or 30 drinks of whiskey or the like/mo; heavy drinkers were defined as those who drank more than this amount. The relative age adjusted risks for mouth cancer among light drinkers and nonsmokers, non-drinkers and smokers, light drinkers and smokers, and heavy drinkers and smokers were: 1.16, 3.22, 4.03, and 10.35, respectively. The corresponding risk values for tongue cancer by the same categories were: 1.35, 2.02, 3.51, and 10.87, respectively. When the effect of age shift on the chi-square value for age-adjusted relative risks for mouth cancer was examined, women who were light drinkers and smokers were susceptible to the onset of mouth cancer 12.5 yr earlier than abstainers (at the 5% probability level). Women who were heavy drinkers and smokers showed a 20-yr shift in onset, even at the 1% probability level. Women who smoked but did not drink showed a 10-yr shift in age of mouth cancer onset. Similar results were obtained for women with tongue cancer, except for those who smoked but did not drink; this latter group was not significantly different from abstainers. Exposure to alcohol only did not produce any clear shifts in age of cancer onset for either mouth or tongue cancer. The combined effects of smoking and drinking appear to be particularly significant in terms of the age of intraoral cancer onset. (15 Refs)

52. ASSOCIATION OF CANCER SITES WITH TOBACCO AND ALCOHOL CONSUMPTION AND SOCIOECONOMIC STATUS OF PATIENTS: INTERVIEW STUDY FROM THE THIRD NATIONAL CANCER SURVEY.

Williams RR, Horm HJ
Dept. Internal Medicine, Univ. Utah Coll. Medicine, Salt Lake City, Utah, 84121
J Natl Cancer Inst; 58(3):525-547 1977

From personal interviews obtained for 7,518 incident cases of invasive cancer from the population-based Third National Cancer Survey, the quantitative lifetime use of cigarettes, cigars, pipes, unsmoked tobacco, wine, beer, hard liquor, and combined alcohol were recorded, as well as education and family income level. In an initial screening analysis of these data, Mantel-Haenszel 2 x 2 contingency tabulations and multiple regression analyses were used to compare each specific cancer site with controls from other sites to test for association with the 'exposure variables.' Significant positive associations with cigarette smoking were found for cancers of the lung, larynx, oral cavity, esophagus, stomach, pancreas, bladder, kidney, and uterine cervix. Other forms of tobacco were associated with cancers of the oral cavity, larynx, lung, and cervix. Consumption of wine, beer, hard liquor, and all combined showed positive associations with neoplasms of the oral cavity, larynx, esophagus, colon, rectum, breast, and thyroid gland. College education and high income both showed positive associations with cancers of the breast, thyroid gland, uterine corpus, and melanomas in males. These same indicators of high socioeconomic status showed inverse associations with invasive neoplasms of the uterine cervix, lung lip-tongue, and colon in females. College attendance (but not income) showed an inverse association with stomach cancer and positive association with pancreatic cancer in males. Still other tumor sites showed 'suggestive' associations with each of these exposure variables. In the analyses producing these results, age, race, sex, smoking, drinking, education, income, parity, foreign birth, marital status, and geographic location were used as stratification variables separately or in combination when appropriate to assess and control for their potentially confounding affects and to examine results in different strata to assess interaction. (Author abstract) (41 Refs)

53. DIFFERENCES IN SEX RATIO ACCORDING TO CANCER SITE AND POSSIBLE RELATIONSHIP WITH USE OF TOBACCO AND ALCOHOL. REVIEW OF 65,000 CASES.

Flamant R, Lasserre O, Lazer P, Leguerinais J, Denoix P, Schwartz D
Gustave-Roussy Inst., Villejuif/Seine, France
J Natl Cancer Inst; 32(6):1309-1316 1964

In a study of 65,000 cases of cancer where data on etiology and site were available, the male/female sex ratio was very high for those sites with a very strong association with the use of both tobacco (T) and alcohol (A): hypopharynx, 28.0;

larynx 27.4. Where the association with T was very strong and that with A strong, sex ratios were: oropharynx, 11.6; oral cavity (sites other than tongue and lips), 8.6. Where the reverse relationship held, sex-ratios were: esophagus, 16.6; tongue, 9.3. With lungs where a strong relationship to T only was noted, sex ratio was 11.8. Where a strong relationship to T only was noted sex ratio for lips was 8.1, for bladder and other urinary organs, 2.6. While no relation to A and T was seen with the stomach, the sex ratio for the cardiac portion was clearly higher than for all other regions of the stomach.

54. PROGNOSTIC EFFECT OF TOBACCO AND ALCOHOL USE IN PATIENTS WITH ORAL TONGUE CANCER.

Johnston WD, Ballantyne AJ
Ellis Fischel State Cancer Hosp., Business 70 and Garth Ave., Columbia, MO 65201
Am J Surg; 134(4):444-447 1977

Of 351 patients with oral tongue cancer, 96/308 chronic users of tobacco and/or alcohol were dead from their tumor within 5 yr, compared with only 6/43 nonusers. In addition, nonusers were older than the users when they developed the disease. Second primary cancers developed in 27.4% of the users but in only 18.5% of the nonusers. (6 Refs)

55. ALCOHOL, TOBACCO AND AGE FACTORS IN THE RELATIVE FREQUENCY OF CANCER AMONG MALES WITH AND WITHOUT LIVER CIRRHOSIS.

Keller AZ
Veterans Admin. Central Office, 151G, Dept. Medicine and Surgery, 810 Vermont Ave., NW, Washington, DC 20420
Am J Epidemiol; 106(3):194-202 1977

Data on white men with cancer only (Group A, 374 patients) or cancer plus liver cirrhosis (Group B, 286 patients) were analyzed to determine whether the patient groups differed significantly by age, relative frequency of cancers by site, and the daily use of tobacco and alcohol. Among the Group B patients, the liver cirrhosis was usually diagnosed 4 yr or more before squamous cell carcinoma of the mouth, pharynx, or larynx; most digestive organ cancers were diagnosed concurrently with the cirrhosis. Oral, pharyngeal, respiratory, digestive, genitourinary, and skin cancers were seen 3-4 yr earlier in Group B than in Group A. Only cancers of the mouth, pharynx, and digestive system were significantly excessive among Group B patients. Risk factors in liver cirrhosis such as the excessive use of whiskey, tobacco plus alcohol, and mixed alcoholic beverages were positively associated with cancers of the oral cavity and liver. The relative frequency of cancer of the floor of the mouth and liver was increased significantly in Group B patients who also smoked and drank heavily. When cancer patients of both groups smoked and drank in comparable amounts, floor of the mouth and liver cancers were still significantly excessive among Group B patients. Since glycogen is stored and metabolized at both tissue sites, glucose metabolism is speculated to be a common factor in the pathogenesis of these two cancers. (13 Refs)

56. EPIDEMIOLOGY OF ALCOHOL AND CANCER.

Tuyns AJ
Unit Epidemiology and Biostatistics, International Agency Res. Cancer, 150 Cours Albert Thomas, 69372 Lyon Cedex 2, France
Cancer Res; 39(7,part2):2840-2843 1979

Both prospective and retrospective epidemiological studies indicate that alcohol consumption is a cancer hazard. Prospective studies of excessive drinkers have shown an increased risk for cancer of the mouth, pharynx, larynx, esophagus, liver, and lung. Retrospective studies have confirmed this excess risk. For cancers of the buccal cavity, pharynx, larynx, and esophagus, the effect of drinking has been shown to be associated with the effect of smoking. In the case of esophageal cancer, these two effects are independent, and the observations made are consistent with a multiplicative model. Primary liver cancer is also associated with alcohol consumption, probably by a less direct action; the importance of the impact of alcohol on primary liver cancer is probably underestimated. Animal experiments have not shown that ethanol alone has a carcinogenic effect, and the mechanisms by which alcoholic beverages act on humans remain unknown. The proportion of cancer cases at sites known to be associated with alcohol consumption is approx 8% in most population groups in the US. This indicates that a sizeable proportion of cancers is potentially preventable if appropriate action is taken. (29 Refs)

57. ALCOHOL AND CANCER.

Tuyns AJ
International Agency Res. Cancer, Lyons, France
Alcohol Health Res World; 2(4):20-31 1978

The role of alcohol in the development of cancer, particularly cancer of the mouth, tongue, larynx, pharyns, esophagus, liver, and lung, is reviewed. Alcohol consumption has also been associated with stomach, pancreatic, and rectal cancer. In some of these cancers, the effects of drinking and smoking are usually combined in an additive or even multiplicative manner. (108 Refs)

58. ALCOHOL AS A CO-FACTOR IN THE ETIOLOGY OF CANCER.

Schottenfeld D
Dept. Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 43(5,Suppl):1962-1966 1979

Alcohol and tobacco appear to act synergistically in the pathogenesis of epithelial cancers of the oropharynx (excluding lip), larynx, and esophagus. For the subsites within the upper aerodigestive tract, over 10,000 deaths in United States men during 1978 may be attributed to tobacco and alcohol consumption. The cancer sites for which tobacco and alcohol are major determinants occur with greater frequency in men, blacks, lower socioeconomic groups, and with increasing urbanization and increasing age (35-70 yr). Because primary hepatocellular carcinoma occurs more commonly in patients with cirrhosis, chronic alcohol abuse is an important risk factor for carcinoma of the liver parenchyma. Although experimental animal studies have failed to demonstrate whether ethanol can independently initiate tumorigenesis various alternative or associated biochemical and immunological mechanisms of action have been proposed to explain the effects of alcohol consumption on cancer incidence. (39 Refs)

59. EPIDEMIOLOGICAL OPPORTUNITIES IN ALCOHOL-RELATED CANCER.

Fraumeni JF
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205
Cancer Res; 39(7,part2):2851-2852 1979

Epidemiological studies have clearly deomonstrated that alcohol interacts with tobacco smoke in the development of cancers of the oropharynx, esophagus, and larynx. It should be possible to clarify further the role of alcohol itself, the modifying effects of tobacco, dose-response relationships, and nutritional cofactors. Studies are also needed to delineate the steps by which alcohol consumption leads to liver cancer and to resolve the suggestion that certain beverages may predispose to other cancers, including those of the pancreas and rectum. Epidemiological investigations should be combined with experimental work to identify hazardous fractions in alcoholic beverages and to delineate the mechanisms by which alcohol promotes carcinogenesis. Epidemiologists and biometricians may also contribute toward the development of programs aimed at primary prevention and early detection of cancers related to alcohol and tobacco. Incorporation of research questions into data collection systems deserves serious consideration as a means of obtaining additional valuable information for etiological studies. (no Refs)

60. THE EFFECT OF ALCOHOL CONSUMPTION ON RISK OF CANCER OF THE HEAD AND NECK. (PP. 51-55)

Rothman KJ
677 Huntington Ave., No. 802, Boston, MA 02115
Head and Neck Cancer. State of the Art Conference, February 16, 17 and 18, 1976. Vol.88, St. Louis, MO, Laryngoscope, No. 1, Part 2, Suppl. 8, 1978.

Alcoholics are at increased risk for the development of oral cancers. It is estimated that alcohol plays an etiological role in greater than 50% of the oropharyngeal cancers in the US. The sites most affected are those that come into direct and prolonged contact with the alcohol, the floor of the mouth and the tongue. The risk from joint exposure to alcohol and tobacco is about 2.5 times the risk expected if the effects of the two substances were additive; a synergistic effect is thus apparent. Although education of the public on the increased risk of oral cancers from alcohol and tobacco use is important, screening programs for at-risk patients would have a more beneficial effect. Research should focus on whether carcinogens in tobacco smoke dissolve in the alcohol and are thus held in more prolonged contact with the oral mucosa or whether certain congeners in the alcohol exert a special effect.

61. RELATIONSHIP OF DRINKING TO HEAD AND NECK CANCER.

Feldman JG, Boxer P
Dept. Preventive Medicine and Community Health, SUNY Downstate Medical Center, 450 Clarkson Ave., Box 43, Brooklyn, NY, 11203
Prev Med; 8(4):507-519 1979

The possible mechanisms of alcohol carcinogenicity were investigated in a group of 185 men with head and neck cancer in sites known to be correlated with smoking and/or drinking and in a control group of 182 men with cancer in sites not associated with smoking or drinking. Head- and neck-cancer sites were further divided into 'high' and 'low' probability categories based upon the likelihood of direct contact of the site with alcohol in its liquid form. In comparing the drinking and smoking behavior of the test patients versus controls (figures adjusted for alcohol use), consumption of more than one pack of cigarettes/day resulted in a 7-9 x increased risk of cancer for both high- and low-probability sites. When figures were adjusted for smoking habits of the test and control individuals, daily consumption of greater than 6 ounces of whiskey or its equivalent was associated with a significant (4.5 x) increased risk of cancer in the high-probability sites; there was no significant increase in risk in the low-probability sites. Overall, the risk of developing a head- and neck-cancer site was 18 x greater for a patient who both smoked and drank heavily than for an abstainer. The av age of diagnosis of heavy smokers and drinkers was 9 yr earlier than the av age of non-heavy users of these substances, and regression analysis indicated that the patients with cancer in high probability sites showed correlations between age at diagnosis and two other factors: alcohol consumption and age at first drinking. These results are consistent with the hypothesis that alcohol carcinogenicity is related to the direct contact of alcohol and tobacco with the involved site. (21 Refs)

62. ETIOLOGICAL AND PREVENTIVE IMPLICATIONS IN ALCOHOL CARCINOGENESIS.

McCoy GD, Wynder EL
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Cancer Res; 39(7,part2):2844-2850 1979

The current state of knowledge of the epidemiological association of alcohol and tobacco consumption with cancers of the head and neck in humans is reviewed. There are four possible mechanisms that can be envisioned for the association between alcohol and cancer: alcohol as a solvent, alcohol-induced increases or decreases in liver metabolism, or alcohol-induced alterations in target tissue metabolism. The possible involvement of alcohol-associated nutritional deficiencies in the etiology of head and neck cancer is considered. Data are presented that indicate that the in vitro metabolism of the hepatocarcinogen N-nitrosopyrrolidine is increased in microsomal fractions isolated from ethanol-consuming hamsters. Relevant studies in experimental animals are discussed in the context of possible mechanisms that could account for the increased risk of cancer in heavy drinkers who smoke. (118 Refs)

63. ALCOHOL. (PP. 139-150)

Rothman KJ
Persons at High Risk of Cancer, an Approach to Cancer Etiology and Control. Fraumeni Jr. JF, ed. New York, Academic Press, Inc, 554 pp., 1975.

Cancer of specific sites and an increased overall cancer risk attributable to alcohol consumption are reviewed and the prospects for control discussed. Alcohol and tobacco are estimated to account for approximately 3/4 cancers of the oral cavity in U.S males. The risk of combined heavy smoking and drinking is 15 times as great as that for non-smokers/drinkers, whereas the risk from heavy smoking alone is only 2 to 3 times as great. Alcohol consumption, particularly heavy whiskey consumption, elevates the risk for laryngeal cancer more than 10 times compared to abstinence or moderate drinking. In a study restricted to moderate smokers, it was found that heavy drinkers experienced a risk of esophageal cancer more than 25 times that of nondrinkers. Because the geographic variation of esophageal cancer is exceptional and alcohol consumption is nearly ubiquitous, other factors probably have an important function. The carcinogenic agent elevating the risk in alcohol drinkers may not be alcohol but a contaminant. In cohort studies of alcoholics no excess of stomach cancers was observed, but the distinctive clinical and epidemiologic features of cancer of the gastric cardia, in addition to its reported association with alcohol consumption, indicate that at least some cases may be linked to alcohol consumption. Primary cancer of the liver occurs with great frequency (10%-30%) among alcoholics with cirrhosis. A correlation analysis of age-adjusted mortality data and beer consumption revealed a high correlation between death from rectal cancer and beer consumption, but this association is considered tentative until it can be established in studies with individuals. Heavy drinkers have an estimated 20%-30% increase in cancer risk over nondrinkers and moderate drinkers. To the extent that alcoholics can be approached as a group, it seems advisable to implement trial screening programs to evaluate the potential benefit of early cancer detection and treatment.

64. ETIOLOGY AND EPIDEMIOLOGY OF CANCER OF THE MOUTH AND PHARYNX IN SWITZERLAND.

Junod B, Pasche R
Institut universitaire de medecine speciale et preventive, Hopital Sandoz, CH-1011 Lausanne, Switzerland
Schweiz Med Wochenschr; 108(24):882-887 1978

The epidemiology and etiology of cancer of the mouth and pharynx in Switzerland were studied. The incidence is 6.4/100,000, which is considerably higher than in most other industrialized countries (1.4-4.9/100,000), but significantly lower than in France (13.1/100,000). The male/female ratio is 7.4, which is comparable to that in countries with high overall incidence. Cancers of these sites mostly affect relatively young men. An etiological survey of 226 patients revealed a correlation between cigarette smoking and alcohol consumption on one hand, and the incidence of cancer of the mouth and pharynx on the other hand. Smokers smoking greater than or equal to 10 cigarettes a day accounted for 87.9% of the 226 patients, while nonsmokers accounted for 6.8% only. Persons consuming greater than or equal to 5 deciliters of wine daily accounted for 82% of the 226 patients. The cancer incidence was highest among smokers who were also heavy drinkers. While ethanol proper is not carcinogenic, it facilitates the penetration of carcinogenic substances through the mucosa. It seems likely that some alcoholic beverages available in Switzerland contain carcinogenic substances. The findings suggest that the beverages consumed by the cancer patients and those consumed by controls should be tested for mutagenicity. (32 Refs)

65. PREMATURE MORTALITY ATTRIBUTABLE TO SMOKING AND HAZARDOUS DRINKING IN CANADA.

Ouellet BL, Romeder JM, Lance JM
Long Range Planning Directorate, Dept. Natl. Health and Welfare, Jeanne Mance Building, Tunney's Pasture, Ottawa, Ontario K1A OK9, Canada
Am J Epidemiol; 109(4):451-463 1979

All 1974 causes of death in Canada related to smoking and hazardous drinking were reviewed, and the extent of premature mortality in Canada attributable to each of these two risk factors was determined. For each cause, existing epidemiologic data were analyzed and used to determine the fraction of premature mortality that could be attributed to each factor (attributable fraction, AF). This fraction was then multiplied by the corresponding Canadian premature mortality measured in terms of deaths between ages 1 and 70 and potential years of life lost (PYLL) between ages 1 and 70, which gives a higher wt to younger deaths. In overall importance in terms of deaths or PYLL attributable to current smoking, lung cancer ranked second (2,655 deaths, AF 63.4%). In terms of fraction of total deaths and PYLL attributable to current smoking, cancer of the oral cavity and pharynx, larynx, and esophagus ranked first (AF 66%), but this joint cause represented relatively few actual deaths (563) and PYLL compared to the two leading causes, ischemic heart disease (4,531 deaths) and lung cancer. Cirrhosis of the liver ranked second (after alcoholism and alcoholic psychosis, AF 100%) in terms of the fraction of deaths (AF 68%) and PYLL attributable to hazardous drinking, but it was surpassed only by moter vehicle accidents in terms of actual numbers of attributable deaths and PYLL (1,502 vs 2,212 deaths). In terms of number of deaths and PYLL attributable to hazardous drinking, cancer of the oral cavity and pharynx, larynx, and esophagus ranked fifth (AF 21.7%). Regardless of whether premature mortality is expressed in terms of deaths or PYLL, about 18% of Canadian premature mortality is attributable to current smoking and/or drinking (with the range of possible values being 14%-22%). (34 Refs)

66. INCIDENCE OF CANCER OF THE BUCCAL CAVITY IN THE CANTONS OF GENEVA AND NEUCHATEL, ESPECIALLY IN MEN.

Obradovic M, Roch R, Pellaux S
Registre Genevois des Tumeurs, Geneva, Switzerland
Rev Med Suisse Romande; 99(2):63-65 1979

The incidence of cancer of the buccal cavity was studied in the cantons of Neuchatel and Geneva. The crude incidence per 100,000 subjects in the canton of Neuchatel was 16 for men and 4.9 for women during 1972-1975. The corresponding figures for the canton of Geneva during 1970-1975 were 20.9 and 5.0. The risk of cancer of the buccal cavity or pharynx was found to be 1/300 men under the age of 65 yr, and 1/200 men under the age of 75 yr. In the male population of the canton of Geneva, the incidence of cancer of the tongue, buccal cavity, oropharynx, and hypopharynx was 3.6, 4.3, 5.7, and 4.9, respectively. In Western Europe, the incidence of cancer of the tongue, buccal cavity, oropharynx, hypopharynx, and esophagus is highest in the canton of Geneva. The use of tobacco and/or alcohol, is considered a risk factor. (4 Refs)

67. HEAD AND NECK CANCER IN ALCOHOLICS. THE RELATIONSHIP TO DRINKING, SMOKING, AND DIETARY PATTERNS.

Kissin B, Kaley MM, Su WH, Lerner R
Div. Alcoholism and Drug Dependence, Dept. Psychiatry, Downstate Medical Center, Univ. New York, 600 Albany Ave., Brooklyn, NY, 11203
JAMA; 224(8):1174-1175 1973

Three thousand and seven alcoholics were examined for head and neck abnormalities and interviewed about drinking, smoking and dietary patterns. Results indicated (1) the alcoholics had significantly more cancer cases than the controls, (2) the head and neck cancer incidence rate for alcoholics was higher than for the general population (286.5 vs 53.9/100,000), and (3) the alcoholics with head and neck cancer were heavy drinkers and smokers for significantly longer periods of time than the alcoholics without head and neck abnormalities. (Author abstract) (11 Refs)

68. THE EPIDEMIOLOGY OF ORAL CAVITY, PHARYNGEAL AND ESOPHAGEAL CANCER OUTSIDE OF NORTH AMERICA AND WESTERN EUROPE.

Mahboubi E
Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NB 68105
Cancer Suppl; 40(4):1879-1886 1976

Geographical variations in the incidence of oral cavity, pharyngeal, and esophageal cancer were studied, with special reference to the rates in Africa, Asia, Eastern Europe, and South America. Although reporting techniques differ greatly and comparisons must be made with caution, significant variations are evident. The roles of known environmental carcinogens, such as N-nitroso compounds and polycyclic aromatic hydrocarbons, and of cultural habits, such as smoking or chewing tobacco and excessive consumption of alcoholic beverages, in the etiology of these cancers are discussed. (45 Refs)

69. EXCESS MORTALITY OF MEN IN FRANCE. ANALYSIS OF MEDICAL CAUSES OF DEATHS.

Riondet J
No affiliation given
Rev Prat; 29(22):1819-1820 1979

The excess cancer mortality of French men over women in the age bracket 40-60 yr is significantly higher than that in the US and, especially, in Sweden. The mortality due to tumors of the buccal cavity, pharynx, esophagus, and larynx is 5-17 times higher than that in Sweden and 4-5 times higher than that in the US. Alcohol and smoking are considered causes of the excess cancer mortality. (2 Refs)

70. EPIDEMIOLOGY OF HEAD AND NECK CANCER.

Rothman KJ
Dept. Epidemiology, Harvard Univ. Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
Laryngoscope; 88(3):435-438 1978

Epidemiological factors associated with cancers of the lung, larynx, esophagus, and mouth are reviewed. Environmental contaminants such as asbestos, radon gas, arsenic, chromium, coal products, iron oxide, mustard gas, nickel, and petroleum account for many lung cancers, but the major environmental cause is cigarette smoking (80%-90% of all cases). The risk of lung cancer is positively related to the number of cigarettes smoked per day, extent of inhalation, and number of smoking years. Studies have suggested that aryl hydrocarbon hydroxylase inducibility may be a susceptibility factor for the action of tobacco smoke. Laryngeal cancer is also related to cigarette smoking, but cigar and pipe smoking and alcohol consumption are also associated with the disease. Recent data suggest that the risks associated with smoking and alcohol consumption are synergistic. Cancer of the esophagus has certain geographic variations, but the incidence in the US appears to be associated with alcohol consumption. It is possible that contaminants in the alcoholic beverage, and not ethanol per se, play a role in cancer development. Oral and pharyngeal cancers are associated with alcohol and tobacco use, and it is estimated that these two risk factors combined account for 75% of all oral cavity cancers in US men. A synergistic action may also exist. It is estimated that already identified risk factors account for greater than 90% of new head and neck cancer cases and that tobacco alone is related to approx 80% of all these cancers in the US. (10 Refs)

71. A RETROSPECTIVE STUDY OF RISK FACTORS RELATED TO ORAL CANCER IN WOMEN (MEETING ABSTRACT).

Hayes RB, Matanoski GM, Bross ID
Johns Hopkins Univ., Sch. Hygiene and Public Health, Baltimore, MD 21205
Am J Epidemiol; 106(3):230 1977

This case-control study of oral cancer utilized data collected on women upon admission to Roswell Park Memorial Institute, Buffalo, New York, between 1957 and 1966. The series included 201 cases with diagnosed oral cancer and 1988 non-neoplastic controls. The data were analyzed by age and by the consumption of alcohol and cigarettes as related to the risk of developing oral cancer. The relative risk of developing oral cancer with regard to tobacco exposure was found to be age dependent. Alcohol consumption, alone, did not increase the risk to a significant degree, nor in the group age 60+ did it markedly affect the risk in conjunction with cigarette use beyond the risk due to smoking alone. The results are discussed and contrasted with the results found in previous studies. (Author abstract) (no Refs)

72. GENERAL AND ETIOEPIDEMIOLOGICAL CHARACTERISTICS OF CANCER OF THE UPPER RESPIRATORY AND DIGESTIVE TRACTS.

Cachin Y
Departement de chirurgie cervico-faciale et ORL, Institut Gustave-Roussy, 16 bis, avenue Paul-Vaillant-Couturier, 94800 Villejuif, France
Rev Prat; 28(31):2359-2364 1978

According to statistics compiled in 1967, cancers of the upper respiratory and digestive tracts (URD) represent 12% of all cancers and 8% of cancer deaths in France. The epidemiology of URD cancers is discussed on the basis of 5,748 patients observed at the Gustave-Roussy Institute from 1959 to 1970. Approx 95%-97% of these patients were men. A high proportion of patients with cancers of the tongue, oropharynx, hypopharynx, and esophagus were alcoholics. Alcoholics did not have a high incidence of cancers of the nasal cavity and sinuses or the rhinopharynx. Cancers at these sites were more likely to occur among persons in certain occupations, such as woodworkers, carpenters, asbestos miners, and nickel workers. Heavy smokers tended to develop cancers of the same areas as alcoholics in addition to cancers of the lung, lip, and buccal cavity. Again, tobacco usage was not strongly associated with cancers of the upper respiratory tract, such as the nasal cavities and rhinopharynx. URD cancers have a varied incidence in relationship to geographical region and sex. Examples of these variations are provided. (no Refs)

73. CANCER OF THE ORAL CAVITY IN NEGROES.

Leffall LD, White JE
Dept. Surg., Howard U., Washington, D. C.
Surg Gynecol Obstet; 120(1):70-72 1965

In a 15-yr survey of oral cancer in a total of 107 Negroes (17-86 yr old, av. 53 yr; 72% male), the primary sites in order of decreasing frequency were: the floor of the mouth, tonsil, and tongue: carcinoma of the lip was rarest (2/107 = 1.8%). Squamous cell carcinoma was the most common tumor type. Metastatic cervical adenopathy (usually involving the submaxillary and subdigastric nodes) was initially present in 63% of patients Chronic alcoholism, prolonged use of tobacco (usually cigarettes), and poor oral hygiene were prominent associated factors in this patient series. Among the 7 patients with buccal mucosa cancer, 4 used chewing tobacco.

74. SQUAMOUS CELL CARCINOMA OF THE FLOOR OF THE MOUTH.

Ballard BR, Suess GR, Pickren JW, Greene GW, Shedd DP
Dept. Pathology, Meharry Medical Coll., 1005 18th Ave., N., Nashville, TN, 37208
Oral Surg; 45(4):568-579 1978

The clinical and biologic behavior of squamous cell carcinoma of the floor of the mouth was studied in 100 patients (81 men and 19 women). Ninety-four were Caucasians and six were Negroes; the age range was 33-85 yr, with an av of 63 yr. The peak incidence in women was in the 50 to 59 yr age group; in men, there was equal frequency in each age group greater than 50 yr. A total of 43/89 patients diagnosed within 1 yr of the onset of symptoms had regional lymph node metastases. The 5-yr survival rate decreased from 86% to 0% as the stage of disease progressed from I to IV. Thirty-three patients developed a total of 83 other primary cancers, and 72 of these arose in the upper alimentary and respiratory tracts. The oral carcinomas were classified as follows: well differentiated (49), well to moderately differentiated (7), moderately differentiated (20), moderately to poorly differentiated (10), poorly differentiated (2), and unspecified (12). Fifty-eight patients were heavy smokers, 33 were heavy drinkers, 28 were both heavy smokers and heavy drinkers, and 21 were nonsmokers and non-drinkers.

75. NUTRITIONAL AND ENVIRONMENTAL FACTORS IN CARCINOGENESIS (MEETING ABSTRACT).

Wynder E
American Health Foundation, New York, N.Y.
Arnold O Beckman Conference on Biochemistry of Cancer held in San Antonio, September 6-8, 1978. American Association for Clinical Chemistry, San Antonio, TX, 1978.

Nutritional factors are increasingly incriminated as playing a role in the causation in man. While food additives and contaminants have received a great deal of public attention in nutritional carcinogens, present evidence indicates that nutritional deficiencies and particularly nutritional excesses play important roles in the development of certain types of human malignancies. This present discussion will limit itself to three examples in this area. It will review the evidence that alcoholism, probably on the basis of nutritional deficiency, enhances the risk of smokers to develop cancers of the oral cavities, larynx and esophagus. We will present epidemiological, metabolical, and experimental evidence detailing the importance of nutrition, particularly in terms of total fat calories in epidemiology in cancer of the breast and cancer of the colon. The discussion will finally deal with some suggestions as to preventive measures that could be aimed at high risk populations as well as the population as a whole. (3 Refs)

76. ETIOLOGICAL ASPECTS OF SQUAMOUS CANCERS OF THE HEAD AND NECK.

Wynder EL
Amer. Hlth. Found., New York, N. Y.
JAMA: 215(3):452-453 1971

Various environmental factors associated with squamous cell cancer of the head and neck were reviewed. A close association has been established between tobacco usage and squamous cell cancer of the head and neck in virtually all sites. Cancer of the vocal cords was found to be predominantly related to cigarette smoking, while other head and neck cancers including cancers of the oral cavity and pharynx, are equally strongly associated with pipe and cigar smoking. Data from India have indicated that tobacco and betel nut chewing is causally related to cancer of the mouth. In women, oral cancer was usually found to be located in the tongue or buccal mucosa. Cancer of the head and neck in sites other than the lip and vocal cord was strongly related to heavy alcohol consumption; however, the fact that most heavy drinkers also smoke made it difficult to assess the relative weights of smoking and drinking as etiological factors for these conditions. While no evidence that alcohol is carcinogenic per se exists, it was suggested that alcohol may potentiate the carcinogenic effects of tobacco smoke. Syphilis has been correlated with cancer of the anterior 2/3 of the tongue; and liver cirrhosis has also been correlated with cancer of the upper alimentary tract. The correlation of Plummer-Vinson's disease brought on by iron deficiency and cancer of the squamous tissue of the mouth and pharynx may suggest that cancer of the head and neck are sometimes associated with deficiency conditions. It has been shown that riboflavin deficiency can lead to atrophy and hyperkeratosis in the upper alimentary tract. The skin of riboflavin-deficient mice was found to be more susceptible to carcinogenic agents than the skin of normal mice. Heavy cigarette smoking apparently makes patients more likely to develop a second primary tumor in the oral cavity and upper respiratory tract. Furthermore, cessation of smoking and drinking after the appearance of the first primary tumor did not ensure that a second primary tumor will not develop.

77. CULTURAL AND BEHAVIORAL ASPECTS OF RISK FACTORS: SOCIETY'S OBLIGATION.

Wynder EL
American Health Foundation, 1370 Ave. of the Americas, New York, NY, 10019
J Environ Pathol Toxicol; 1(2):11-18 1977

Individual and societal actions that could be taken to reduce cancer risk are considered. The reduction of tobacco smoking should be approached from three areas: (1) education, (2) smoke cessation programs, and (3) development of a less harmful cigarette. Individual preventive action with regard to nutrition can be effected by reducing the intake of whole milk, butter, and meat, especially beef. In terms of managerial preventive medicine, the reduction of fat in all dairy products and in beef is recommended. More research is needed to determine the extent to which, if any, vitamin or mineral deficiencies relate to specific cancers. Heavy alcohol consumption has been established as a risk factor for cancer of the mouth, larynx, and esophagus, primarily in smokers. This promotional effect of alcohol is probably related to nutritional deficiencies, a dietary condition commonly associated with excessive alcohol intake. Occupational exposures are estimated to be related to less than 5% of total cancer incidence among men and less than 1% among women. Nevertheless, every occupational cancer death should be and possibly could be avoided. Agents in the workplace that may increase cancer risk should be eliminated or reduced to an acceptable minimum. (11 Refs)

78. DIET AND CANCER.

Hirayama T
Epidemiology Div., Natl. Cancer Center Res. Ins., Tokyo, Japan
Nutr Cancer; 1(3):67-81 1979

Data from a series of Japanese studies concerning the effect of diet on cancers of the lung, esophagus, stomach, colon, breast, and cervix are reviewed. The risk of lung cancer in smokers and nonsmokers was reduced by consumption of green-yellow vegetables (GYV), and among ex-smokers, reduction in lung cancer risk with time after cessation of smoking was greater among those who consumed GYV daily than among others. Vitamin A must be the most important factor in any protective effect of GYV, followed by vitamin C. GYV consumption had a similar, but weaker effect on colon, stomach, and prostate cancers. The risk of esophageal cancer was increased in those who smoked and consumed alcohol, the risk increasing with the alcohol content of the beverage consumed. The risk of esophageal cancer was also increased by the combined intake of bracken fern and hot tea gruel. Stomach cancer was lowest in persons consuming two glasses of milk daily, and the amount of fiber consumed was negatively correlated with colon cancer mortality. Daily meat intake had no effect on colon cancer risk, but daily meat consumption was associated with increased breast and pancreatic cancer risks. Breast cancer mortality was positively correlated (r = 0.842) with daily fat intake. The risk of cervical cancer was negatively correlated (r = 0.855) vitamin A intake. (17 Refs)

D. Chewing of Tobacco and Betel Nut as Related to Oral Cancer

EDITOR'S NOTE: Abstracts in this category address the chewing of tobacco, betel nut or similar tobacco preparations with or without smoking.

79. QUANTIFICATION OF THE ROLE OF SMOKING AND CHEWING TOBACCO IN ORAL, PHARYNGEAL, AND OESOPHAGEAL CANCERS.

Jayant K, Balakrishnan V, Sanghvi LD, Jussawalla DJ
Tata Memorial Center, Parel, Bombay 400 012, India
Br J Cancer; 35(2):232-235 1977

The proportions of oral, pharyngeal, and esophageal cancers attributable to tobacco smoking and/or chewing and expressed as etiologic fractions were estimated. Based on data for 2,005 cancer patients and an equal number of controls, the overall etiologic fractions were 70% for cancer of the oral cavity, 84% for cancer of the oropharynx, and about 75% for cancer of the hypopharynx and larynx. The fraction was only 50% for esophageal cancer, which indicates that another factor(s) plays an equal role in its etiology. At each of the sites studied, tobacco smoking and chewing acted synergistically, although in varying degrees. (9 Refs)

80. STATISTICAL APPRAISAL OF THE ASSOCIATION OF SMOKING AND CHEWING HABITS TO ORAL AND PHARYNGEAL CANCERS.

Jayant K
Epidemiology Div., Cancer Res. Inst., Tata Memorial Centre, Parel, Bombay-400 012, India
Indian J Cancer; 14(4):293-299 1977

Studies of oral cancer in India are reviewed, and the causal significance of the chewing and smoking of tobacco is examined. The data show that chewing tobacco quid is causally associated with oral cancer and bidi smoking is causally associated with pharyngeal cancer. Tobacco appears to have weak carcinogenic properties, and it needs a co- or syncarcinogen to manifest its potential. Betel nut chewing also appears to have some carcinogenic potential, and evidence suggests that betel nut extract accelerates tobacco carcinogenesis. Bidi smoke contains both benzanthracene and benzo(a)pyrene, at concentrations higher than those in cigarette smoke. Furthermore, a majority of oral, oropharyngeal, and hypopharyngeal cancers can be accounted for by the chewing and smoking of tobacco, actions that interact synergistically. (27 Refs)

81. EVALUATION OF CANCER RISK IN TOBACCO CHEWERS AND SMOKERS: AN EPIDEMIOLOGIC ASSESSMENT.

Jusawalia DJ, Deshpande VA
Bombay Cancer Registry, Indian Cancer Society, Parel, Bombay-12, India
Cancer; 28(3):244-252 1971

A retrospective study of cancer at high risk sites in the region of the head and neck was undertaken at the Bombay Cancer Registry, in 1968, to evaluate the effects of tobacco when chewed or smoked. There is sufficient evidence available today to indict chewing and smoking of tobacco as factors of great importance in the etiology of oral, pharyngeal, laryngeal, and esophageal cancers - the most common sites affected by the disease in Greater Bombay. This cause/effect association is probably as intimate as that of cigarette smoking and lung cancer. The carcinogenic action of chewed tobacco is particularly evident at those sites where the bolus is retained in place for any length of time. Likewise, inhalation of tobacco fumes during the act of smoking produces a stream of gas and of solid particles which impinges directly on the oropharynx and especially on the soft palate initially and exposes smokers to the increased risk of developing cancer at exactly these posterior sites in the oropharynx, rather than more anteriorly in the oral cavity where the tissues do not directly bear the brunt of the onslaught from the smoke. It is revealing to find that the high risk sites involved in tobacco chewers appear to be the least affected in smokers, and vice versa. (Author abstract) (9 Refs)

82. THE PROBLEM OF CANCER IN INDIA: AN EPIDEMIOLOGICAL ASSESSMENT.

Jussawalla DJ
Dept. Surgery, Tata Memorial Cancer Centre, Parel, Bombay, India
Gann Monogr Cancer Res; (18):265-273 1976

Data related to the incidence of various kinds of cancer in different regions of India are presented and compared briefly with the incidences in Connecticut and Japan. In greater Bombay, the overall incidence per 100,000 is 71.8 for men and 67.7 for women and the respective mortality rates per 100,000 are 44.8 and 38.8. The incidence rates in Connecticut are approximately 1.7-1.8 times higher. In Bombay, cancer is the sixth leading cause of death for males and the seventh for females. Among males, oropharyngeal cancer accounts for 49%-73% of all cancers in various districts, while among females genitourinary cancer accounts for 54%-77% (male:female ratio 13:1). Smoking and pan chewing, which have been shown to be associated with oropharyngeal and esophageal cancer, are described briefly. The age-adjusted incidence rates of esophageal cancer for males and females in Bombay are 13.0% and 11.3%, respectively, compared to 5.7% and 1.4% for Connecticut. The age-adjusted incidence rates for stomach cancer for males and females in Bombay are 10.0% and 6.5%, respectively, compared to 14.7% and 6.8% in Connecticut and 95.3% and 44.7% in Japan. The rate of colonic cancer is low, but that of cancer in the rectum and the anal canal is high. It is suggested that elimination of pan chewing and bidi smoking would reduce the incidence of upper alimentary as well as oropharyngeal cancer. Factors associated with an increased incidence of cervical cancer include pregnancy in the middle and late teens and underprivileged social class. The age-adjusted incidence rates of breast cancer in Bombay, Connecticut and Japan are 20.4%, 62.3%, and 11.0%, and the corresponding rates for cervical cancer are 24.7%, 10.3%, and 20.6%. The incidence of breast cancer among Parsi and Sindhi women is higher than in other religions.

83. ORAL AND PHARYNGEAL CANCER IN MADHYA PRADESH.

Gandagule VN, Agarwal S
Med. Coll., Jabalpur, India
J Indian Med Assoc; 53(12):582-585 1969

In Madhya Pradesh, India during the period 1958-1967, there were 814 cases of oral and pharyngeal squamous cell carcinoma which were analyzed according to incidence, site, age, sex, community and histologic features. These 814 cases accounted for 33.8% of all malignancies (48% in males and 18% in females). Estimated incidence rose steeply with age. The av age for hypopharyngeal cancer (52.8 yr) was slightly higher than for oral and oropharyngeal cancer (48.9 yr). Males comprised 72.2% of the cases, females only 27.8%. In the population at risk, Hindus comprised 93.0% and Mohammedans 5.0% of the local population. For both males and females, the incidence of oral and pharyngeal carcinoma was higher in Mohammedans compared to Hindu population; this was attributed to the habit of chewing tobacco. The distribution of oral, oropharyngeal and hypopharyngeal cancer was 63.1%, 20.1% and 16.8%, resp. The buccal mucosa, the base of the tongue and the pyriform sinus were the most commonly affected sites in the oral cavity, oropharynx and hypopharynx, resp.

84. THE EPIDEMIOLOGY OF ORAL AND OROPHARYNGEAL CANCER IN INDIA.

Jussawalla DJ
Tata Mem. Hosp., Bombay, India
Oto-Rhino-Laryngol Tokyo; 206:832-839 1970

The incidence and mortality of oral and oropharyngeal cancer in India was investigated, and a specific etiological factor identified. Age-adjusted incidence rates for cancer of the buccal cavity and pharynx indicate that the Bombay area has the highest worldwide rates for both males and females (38 and 15 cases/100,000 population, resp); these rates were markedly higher than rates for Puerto Rico, the nation with the next highest incidence rates (Puerto Rican rates for males and females, resp. were 24 and 9 cases/100,000 population). Incidence rates for cancer of the lip, salivary glands, gums, buccal mucosa, palate and nasopharynx in Bombay were approximately comparable to rates for other countries; however, females in Bombay appeared to have a slightly higher incidence of lip cancer than females in other countries. Incidence rates for cancer of the tongue and pharynx were higher in Bombay than elsewhere; rates for tongue cancer for males and females in Bombay were 14.6 and 3.3 cases/100,000, compared to 7.1 and 2.1 cases/100,000 for males and females in Puerto Rico. Mortality rates for cancer of the buccal cavity and pharynx were higher in Bombay than elsewhere, with Bombay's rate being 2.4 deaths/100,000 population compared with 2.3 deaths/100,000 for Ceylon and 1.3 deaths for American Caucasians. Tobacco chewing was identified as an etiological factor in oral and oropharyngeal cancer in India, with 72% of oral and oropharyngeal cancer patients being tobacco chewers. Another etiological factor appeared to be abrasion of the back of the tongue by sharp decayed teeth.

85. SOME OBSERVATIONS ON THE ETIOLOGY OF ORAL CANCER.

Khanna NN, Pant GC, Tripathi FM, Sanyal B, Gupta S
Inst. Medical Sciences, Banaras Hindu Univ., Varanasi-221005, India
Indian J Cancer; 12(1):77-83 1975

In a series of 256 cases of oral cancer seen at Varanasi, India, it was found that 90% were addicted to tobacco chewing. There was a distinct pattern of the anatomical distribution of cancer in chewers and non-chewers of tobacco. Patients claimed that the cancer had arisen exactly at the site where they usually kept the tobacco quid. While tobacco was held under strong suspicion as the carcinogenic agent, the role of poor nutrition, bad orodental hygiene and the other ingredients of the betel quid appeared an indirect one. From this study the role of syphilis, tuberculosis, genetic and hereditary factors, endocrine disturbances, occupational and racial factors, and alcoholism could not be substantiated.

86. PATTERN OF MALIGNANCY IN A PLACE IN WESTERN INDIA.

Kirtane JS, Sayed BA, Vaishnav VP
Med. Coll. Baroda, India
Br J Cancer; 24(4):670-672 1970

The incidence of cancer of various sites in a population from Baroda, India was investigated, and it was found that of 4500 cases of malignancy, 25% involved cancer of the bucco-pharynx and 27.8% involved the female genital tract. Buccopharyngeal cancer affected more men than women, and accounted for 39.5% of all malignancies in men and for 4.8% of all malignancies in women. Most female genital tract cancer involved the cervix. Esophageal cancer was the most commonly affected site in the gastrointestinal tract. Most cancers observed were epithelial in origin; sarcomas comprised only 6.2% of the observed malignancies. The high rate of buccopharyngeal cancer in men and its low rate in women may be due to the habit of chewing a mixture of tobacco and lime which is wide-spread among men in this area of India.

87. ORAL AND OROPHARYNGEAL TUMORS.

Wahi PN
Indian Council Medical Res., Ansari Nagar, New Delhi 110016, India
Gann Monogr Cancer Res; 18:19-26 1976

A study of the various factors associated with the occurrence of oral carcinoma was conducted in the Indian district of Mainpuri. The 35-44-yr-old age group had a higher than av frequency of oral cancer, but this was still significantly less than the frequency observed in persons 60 yr old and over. Women developed oral cancer more frequently than men. No differences in the incidence of oral cancer was observed among the different religions. An occupational study revealed a higher occurrence of oral carcinoma among unskilled workers, businessmen, agricultural rent receivers and money lenders. The incidence was found to increase with the level of education up to junior high school, and was higher than average among the literate. The risk of developing oral cancer was eight times greater in persons who chew tobacco daily than in non-chewers. Daily smokers had a risk 2.5 times greater than nonsmokers and those who consumed alcoholic beverages regularly showed a risk 10-fold greater than non-drinkers. Little difference was observed in association with the habit of cleaning the teeth, although people who did not clean their teeth exhibited the highest rate of oral cancer. (2 refs)

88. FURTHER STUDY IN AETIOLOGY OF CARCINOMAS OF THE UPPER ALIMENTARY TRACT.

Shanta V, Krishnamurthi S
W. I. A.), Madras, India
Br J Cancer; 17(1):8-23 1963

The relative frequency of carcinoma of the upper alimentary tract was 34% in Madras and 35.9% in Bombay. Of 882 patients (682 males, 254 females), compared to 400 controls (300 males, 100 females) the site incidence as per cent of all upper alimentary cancers were lip, 2.1%; buccal mucosa (B), 50.5%; anterior 2/3 of tongue, (AT), 9.9%; posterior 1/3 of tongue (PT), 6%; palato-glossal fold, 2%; pharynx (Ph), 15.5%; hypopharynx (HX), 1.5% and esophagus, (E), 12.5%. Cancer of the upper alimentary tract accounted for 40.29% of all malignancies; that of the B, 19%. Betel nut and tobacco chewing was the habit of 83% of males and 85% of females with cancer of the lip and B; 73.9% of males and 50% of females with cancer of the AT; 43.85% of males and 75% of females with cancer of the PT; 35% of males and 43.5% of females with cancer of the Ph; 27.7% of males and 8.3% of females with cancer of the HX; and 42.1% of males and 13.9% of females with cancer of the E; compared to controls, 9.2% of males and 11.2% of females. Heavy use of tobacco in some form for over 20 yr was reported for 100% of males with lip cancers, 98% of B cancers; 92.8% of AT cancers; 98% of PT cancers; 94.7% of oropharyngeal cancers and 82.5% of E cancers; such usage in controls was 60.9%. Comparable values for females were 85.7% (lip); 89% B; 66.7% AT; 100% PT; 60% Ph; and 52.9% E, resp; controls, 11.2%. Dental sepsis was present in approximately 90% of the study group and controls of both sexes; sideropenia in 100% of females with cancer of the HX and cervical E. Exclusion of tobacco chewers lowered the frequency of oral carcinoma to 3.8%, a figure comparable to the frequency in western countries. The fact that females were virtually nonsmokers accounted for the lower incidence of cancer of the upper alimentary tract in them. Hormonal patterns, heredity, race, environment, occupation, pre-existing diseases and pathology were of no etiological significance.

89. ORAL LEUKOPLAKIA IN RELATION TO TOBACCO HABITS.

Mehta FS, Shroff BC, Gupta PC, Daftary DK
Basic Dental Res. Unit., Tata Inst. Fundamental Res., Homi Bhabha Road, Bombay 5, India
Oral Surg; 34(3):426-433 1972

This is a report of a second follow-up study of 3,674 Bombay policemen after 10 yr. One among 117 patients with leukoplakia was reported to have developed oral cancer in the 10-yr period. The 10-yr incidence rate for leukoplakia was 2.8%. Among chewers, the leukoplakia regressed, whereas among smokers, the leukoplakia was found to be more persistent. Although tobacco chewing remained the most prevalent form of tobacco habit, cigarette smoking was found to be on the increase. (Author abstract) (7 Refs)

90. VERRUCOUS SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY.

Fonts EA, Greenlaw RH, Rush BF, Rovin S
U. Miami Sch. Med., Fla.
Cancer; 23(1):152-160 1969

From 1961 through 1966, 160 patients with head and neck tumors were seen at the University of Kentucky Medical Center (Tumor Clinic); 51 had tumors of the oral cavity and 10/51 had verrucous-type tumors (4 additional cases, not included in this group, were diagnosed by the dental school). The histological type was well differentiated squamous cell carcinoma in 5/10 and typical verrucous carcinoma in 5/10. The av age in these 10 patients (5 men, 5 women) was 66.5 yr. (range 53-84); 9/10 were chronic tobacco chewers and 3/9 also used snuff. Other possibly contributory factors included poor oral hygiene; 5/10 wore poorly fitting dentures. All patients were treated by radiotherapy and some also underwent surgery. In 3/10, the slowly growing verrucous carcinomas underwent transformation to more anaplastic forms about 1-7 mo after radiotherapy (which had caused excellent responses at first in 2/3). The marked mucositis usually present during treatment was attributed to the chronic mucosal changes seen in nearly all patients; its relationship to the anaplastic transformation of some of the tumors (possibly induced by ionizing irradiation) could not be determined.

91. BETEL NUT CHEWING AND MOUTH CANCER IN TAIWAN. I. SURVEY OF DISPOSITION OF MOUTH CANCER IN TAIWAN.

Chang KM
Dept. Surg., Nat. Taiwan U. Coll. Med., Taipei, Taiwan
Tumors of the Skin. Cumley RW, McCay J, Aldridge D, Connelly S, Haroz J, Reiner A, White W, ed. Chicago, Year Book Med Publ, Inc, 1964.

Among 89 cases of oral cancer (71 male, 18 female; 18-75 yr, av. 46.5 yr) observed in 1953-1963 at the National Taiwan University Hospital, 92.1% consisted of epidermoid carcinomas, 3.3% of adenocystic carcinoma; 4 (4.6%) cases were diagnosed as leukoplakia. Incidence as to sites was: tongue, 34; gingival and buccal, 16 each; floor of mouth, 9; palate, 7; lips, 2; tonsil, 1. Possible carcinogenic factors were ascertained as follows: venereal disease in 28%; smoking in 82%; wine consumption in 53%; spicy diet in 41%; betel nut chewing in 59%; dentures and caries in 31%. An extensive discussion of the various aspects of the use of betel nuts is included.

92. BETEL NUT CHEWING AND MOUTH CANCER IN TAIWAN (SECOND REPORT).

Chang KM
J Formosan Med Assoc; 65:79-86 1966

The following summary is the result of clinical observation made on the oral mucosa of betel nut chewing people in Formosa. 1) The cases of oral change such as leukoplakia, roughness and redness, so numerous among betel nut chewers, seem undoubtedly due to their habit of continual chewing of the betel quid. In 174 cases of betel nut chewers, the percentages of oral change are over 30% who either do or do not smoke. 2) Frequency of oral change has definite association with the duration of chewing. The cumulative effect of chronic irritation in long duration is obviously more important than the increasing of addict's doses. 3) The exposed surface to irritation of the quid such as buccal, gingiva and lip in mouth angle is more frequent to have lesions. 4) Frequency of oral lesions in 143 control cases who do not chew betel nut reveals only 9%. 5) 136 tobacco smoking cases and 64 wine-drinking cases show only 16 and 22% of oral change respectively. The percentage becomes higher (50%) when they become addicted to betel chewing simultaneously. A survey of Formosan male over the age of 25 years to determine their betel chewing, tobacco smoking and wine drinking habits and the influence of these habits on the development of precancerous changes in the mouth has provided some interesting information. There is sufficient evidence to show that the continual chewing of betel nut plus slaked lime appears to have exerted a definite carcinogenic effect on population in Formosa, even when they do not chew or smoke tobacco. (Author Abstract)

93. THE EFFECTS OF BETEL-NUT CHEWING ON THE BUCCAL MUCOSA: A HISTOLOGICAL STUDY.

Lee KW, Chin CT
Inst. Dental Surg., London, England
Br J Cancer: 24(3):433-441 1970

The histological appearance of leukoplakias from the mouths of West Malaysian betel-nut chewers was examined microscopically. Subjects were Indians and Malays; there were 42 Indians who chewed a quid containing tobacco, and the durations of their chewing habits ranged from 1-50 yr. The remainder of the study population was composed of chewers of quids which did not contain tobacco. An amorphous von Kossa positive layer was seen on the keratin surface in 42 subjects; tobacco was apparently unrelated to this layer. Of 42 tobacco-chewers, 9 showed orthokeratosis, 31 showed parakeratosis, and 12 showed mixed ortho- and parakeratosis. The numbers of non-tobacco-chewers (10 cases) who showed these 3 conditions were resp. 3, 4 and 3. Nine biopsies showed epithelial atypia, all from tobacco-chewing subjects. The average number of mitoses/100 micron length of the basal layer was 0.044 in subjects without leukoplakia and 0.123 in patients with leukoplakia. Long duration of chewing habit seemed to be correlated with relative thinness of buccal epithelium; most chewers whose habit was of 30-40 yr standing had epithelial thicknesses in the 100-250 micron range, while those who had chewed for less than 10 yr were more likely to have epithelia from 450-500 micron in thickness. Eight of the 9 subjects with epithelial atypia had been chewing for more than 10 yr. No relationship between "intensity of habit" (length of time each quid was retained in the mouth of the chewer) and degree of epithelial atrophy was evident. In general, severe histological changes were more likely to be seen in chewers of tobacco-containing quids than in chewers of tobacco-less quids.

94. UPPER ALIMENTARY TRACT CANCER IN NATAL INDIANS WITH SPECIAL REFERENCE TO THE BETEL-CHEWING HABIT.

Schonland M, Bradshaw E
U. Natal Durban Med. Sch.
Br J Cancer; 23(4):670-682 1969

A 1964 surgery of GI cancer in Hindus and Moslems in Durban, Natal indicated a higher incidence of cancer of the upper GI tract (tongue, buccal cavity, pharynx, esophagus and stomach) at all sites in females. Analysis of social habits showed a significant difference in the habit of chewing betel nut between Indian males (8.3%) and females (54.2%) aged 20 or over; the proportion who chewed betel increased with age. The mean age at which betel chewing began was 20-24 yr; more females than males were heavy chewers (more than 4 times/day). No significant difference was found between Hindus and Moslems; the more westernized persons (males and younger person) indulged less in this habit. The major components of the betel quid in this population are betel nut, its leaf and lime; tobacco is added infrequently.

95. BETEL CHEWING CEYLON.

Senewiratne B, Uragoda CG
Dept. Med., U. Ceylon, Peradeniya
Am J Trop Med Hyg; 22(3):418-422 1973

Because the frequency of buccal and esophageal carcinoma may be associated with the common habit of chewing betel leaves, a survey was made to the habit in a large town in Ceylon and the results were analyzed in terms of sex, race, education, and smoking and drinking habits. A representative sample consisting of 1,127 people (aged 15 to more than 75 years) contained 29% who chewed betel. With. regard to esophageal carcinoma in Ceylon, the incidence of betel chewing in 111 cases studied was (81.1%) Therefore, it is likely that betel chewing has some etiological relationship with esophageal carcinoma. There was a striking correlation between the incidence of betel chewing and the educational level with the poorly educated chewing betel more frequently and heavily. The prevalence of betel chewing among the Sinhalese, Tamils, and Moors was 26% to 30% but only 0.8% of the Burghers, with a western cultural background, chewed betel. This rarity of betel chewing among the Burghers is of special interest because buccal and esophageal carcinoma are very rare in this race. Betel chewing was nearly four times as frequent in female as in male Moors. In contrast to western countries, esophageal carcinoma is more common among females. Among all males betel chewing was more frequent among smokers and drinkers, similar in frequency to drinking but only half as frequent as smoking. If the high incidence of buccal and esophageal carcinoma in Ceylon is due to betel chewing, then it is possible that there is a high carcinogenic content in one or more ingredients of the chew.

96. EFFECT OF BETEL CHEWING ON THE ORAL MUCOSA.

Tennekoon GE, Bartlett GC
U. Ceylon, Peradeniya
Br J Cancer; 23(1):39-43 1969

Cancer of the mouth (especially the buccal mucosa) is the most prevalent tumor in Ceylon (42.0% of 5963 tumors seen in 1 hospital from 1937-1942; 27.7% of 9287 tumors seen in the Ceylonese government hospitals in 1963-1964). The effects on the oral mucosa of chronic chewing of betel nut quids containing tobacco leaf were studied in 108 men. These subjects, and 42 male controls who did not chew betel, were nonsmokers; a few men who chewed betel quids without tobacco leaf were excluded. Biopsy specimens of the oral mucosa showed no pathological changes in 43/108 betel chewers and 24/42 controls; the other specimens showed various types of hyperplasia, keratosis, polyposis and/or epithelial downgrowths. Premalignant mucosal changes were seen in specimens from 3/23 men who had chewed of 5 betel quids/day for over 20 yr; these men were in the "cancer age" group. The results suggested that the effects of betel chewing on premalignant changes in the buccal mucosa are negligible, unless the exposure is heavy and prolonged. The 43% frequency of pathological changes in the oral mucosa of nonchewers indicated a role of other factors, such as dietary habits and oral hygiene. The results did not indicate whether dried tobacco leaf is carcinogenic when chewed.

97. OROPHARYNGEAL CANCER IN BHOPAL.

Agarwal V, Arora MM
Dept. Path., Gandhi Coll. Med., Bhopal, India
J Indian Med Assoc; 42(11):519-521 1964

Analysis of biopsy specimens from 519 cases of malignant tumors in Bhopal, India (1958-1961) showed a preponderance of oropharyngeal carcinoma sites (210 patients, 40.5%); of these, a majority (64%) occurred in the buccal mucosa. This site accounted for 53.6%, 20.12% and 16.4%, resp, in Agra, Bombay and Andhra in India, and for 7.9% in the USA. The incidence of carcinoma of the tongue was 7.7% in Bhopal, 31.46%, 27.49%, and 22.8%, resp in Agra, Bombay and Andhra, and 35.94% in the USA. All the Bhopal patients chewed tobacco, betel nut and lime from an early age. This practice is associated with the early incidence of the oral cancers (4th and 5th decades). The malignancies were more common among males (64.4%) than females (35.6%), and among Hindus (83.3%) than Muslims (16.7%). This accords with the habits of the respective populations as regards prolonged tobacco chewing. The predominant histologic type was epidermoid carcinoma (90.5%).

98. MALIGNANT TRANSFORMATION AND NATURAL HISTORY OF ORAL LEUKOPLAKIA IN 57,518 INDUSTRIAL WORKERS OF GUJARAT, INDIA.

Silverman S, Bhargava K, Mani NJ, Smith LW, Malaowalla AM
University of California, School of Dentistry, Division of Oral Biology, San Francisco, CA 94143.
Cancer; 38(4):1790-1795 1976

In Gujarat, India, 6718 industrial workers, over 35 years of age, with oral leukoplakia (confirmed clinically and microscopically), were studied. After 2 years, 4762 (71%) of the individuals were re-examined. The buccal mucosa was the most common site of occurrence; 98.3% of these individuals had oral habits, with smoking alone or smoking in combination with "pan" or "supari" chewing accounting for 74.9% of the habit forms. Six individuals (0.13%) with oral leukoplakia developed oral carcinomas within 2 years. This incidence of malignant transformation was equivalent to 63/100,000 per year, which far exceeds that of new oral cancers expected even in high-risk populations. While 57.3% of the leukoplakic lesions remained unchanged during a 2-year interval, 31.6% disappeared and 11% had an altered appearance. This study confirmed the precancerous nature of oral leukoplakia. (Author Abstract)

99. ORAL CANCER IN 57,518 INDUSTRIAL WORKERS OF GUJARAT, INDIA: A PREVALENCE AND FOLLOWUP STUDY.

Malaowalla AM, Silverman SJ, Mani NJ, Bilimoria KF, Smith LW
Government Dental Coll. and Hosp., Ahmedabad, India
Cancer; 37(4):1882-1886 1976

In Gujarat, India, 57,518 industrial workers over 35 yr old were examined for oral lesions. At a 2-yr interval, 43,654 workers were reexamined. Biopsies were taken from 13,223 lesions. In the initial examination, 29 oral cancers were diagnosed, representing a prevalence rate of 50/100,000. After 2 yr, 22 new oral cancers were diagnosed, representing an incidence rate of 25/100,000/yr. Over 90% were squamous carcinomas, with the majority of lesions occurring in the oropharynx and tongue. All patients who developed squamous carcinomas used tobacco, while 85% of the entire study population habitually used tobacco in some form. Their most common habits were smoking tobacco alone or in combination with chewing "pan"/"supari". Of the carcinomas that developed during a 2-yr interval, 62% appeared in previously normal-appearing mucosa. Leukoplasia was the only oral lesion that proved to be precancerous, with a transformation rate of 0.13% in a 2-yr interval.

100. A STUDY OF 81 CASES OF SQUAMOUS CARCINOMA OF THE BUCCAL AND GINGIVAL MUCOSA.

Mehta MJ
Indian J Surg; 26(4):306-318 1964

In a study conducted in India of 81 patients (60 male, 21 female; av age 47 yr, range 25-70) with squamous carcinoma of the buccal and gingival mucosa, distribution was as follows: 58/81 buccal (30 cheek, 20 cheek + lower jaw, 3 cheek + upper jaw, 5 cheek + upper + lower jaw); 17/81 lower alveolar; 6/81 upper alveolar. Of the 58 buccal cancers, 34 were on the left side, 22 right and 2 lip. Of the 23 alveolar cancers, 12 were on the left, 8 right and 1 center. The most frequent etiologic factor (51/81 patients) seemed to be the chewing of raw tobacco mixed with chunam and keeping it on the same side of the lesion. Pan was chewed by 11/81; leukoplakia was present in many; positive VDRL was seen in 19/81 patients; syphilis occurred in 23%. The relationship of this type of cancer to dental sepsis and stomatitis is also considered.

101. ORAL AND PHARYNGEAL CANCER IN INDIA.

Paymaster JC, Gangadharan P
Tata Mem. Hosp., Bombay, India
CA; 13(2):71-73 1963

In India 35% of all cancer occurs in the oral cavity or pharynx. Among possible precancerous conditions observed by the authors were: leukoplakia (32%) and localized fibrosis affecting the soft and hard palates, the tonsillar fossae and, less frequently, the buccal mucosa. The fibrosis is progressive, leading ultimately to trismus and fixation of the soft palate; carcinoma developed in 30% of such cases. From an analysis of hospital records it is seen that oral carcinoma frequency increases, and oropharyngeal and hypopharyngeal carcinomas decreases as one moves southward. The increase is primarily in cancers of the buccal mucosa. In South and West India it is customary to chew pan (a preparation of tobacco, betel leaf and nut, slaked lime, and spice) which is held in contact with the oral mucosa for hr at a time. In other areas, where carcinomas of the oropharynx and hypopharynx predominate, smoking of bidi (tobacco rolled into a small leaf from a tree of the ebony family), is common. A high frequency of carcinoma of the palate was observed in Andhra Pradesh, where adda poga (smoking the lighted end of a cigar), has been reported. See also CRA 1(2):293, 1963.

102. THE EPIDEMIOLOGY OF ORAL AND OROPHARYNGEAL CANCER. A REPORT OF THE STUDY IN MAINPURI DISTRICT, UTTAR PRADESH, INDIA.

Wahi PN
Sarojini Naidu Med. Coll., Agra, India
Bull WHO; 38(4):495-521 1968

Of 600 new cancer cases seen from March, 1964 to September, 1966, 346 were tumors of the mouth and oropharynx (224/346 of the buccal mucosa). Of the mouth tumors, 121 were seen in 1964, 27/121 from the Mainpuri District (a rural area about 75 miles from Agra). The incidence of mouth cancer in this district was 21.4/100,000/yr. (120.85 in men, 51.15 in women) and increased with age. Among the most significant etiologic factors associated with mouth cancer were tobacco chewing (especially of a local blend of tobacco, slaked lime, betel and powdered cloves or camphor), smoking of very short local cigarettes (2-3 inches long) or cigars, and high consumption of alcohol (especially whiskey). Tobacco chewing from childhood or early adulthood was associated with a high oral cancer risk, but the age when smoking was begun apparently did not affect the risk. The risk was highest in persons who regularly drank and used tobacco in both forms. Oral hygiene and dietary factors (vegetarianism) had no significant effect on the oral cancer risk. The etiologic significance of (socioeconomic status, education, etc) was probably due to their modifying or influencing the use of tobacco and alcohol.

103. AETIOLOGY AND EPIDEMIOLOGY OF ORAL CAVITY CANCERS.

Sidiq Y, Rajagopalan KR, Krishnamurthy MS
Gov. Gen. Hosp., Madras, India
J Indian Med Assoc; 43(11):526-529 1964

Of 13,626 cancers of all sites seen during 1950-1959, 6728 (50%) were of the oral cavity and the distribution by site was as follows: buccal mucosa, 4230; anterior tongue, 864; posterior tongue, 416; alveolus, 407; hard and soft palates, 351; lip, 330; and not classifiable, 130. The male to female sex ratio was 8:3. The peak age incidence was 40-60 yr. (60% of cases). Nearly 95% of the males and 96% of the females were chronic betel nut chewers (with or without tobacco) for 10-20 yr. In this series, 95% of the patients belonged to a very low income group and were in poor general condition. Geographically, nearly 30.3% of the out-patients came from the State of Kerala, about 500 miles away.

104. SYMPOSIUM ON THE CARCINOMAS OF THE MOUTH AND THROAT. (OROPHARYNGEAL CARCINOMA).

Menon AN
Stanley Med. Coll. Hosp., Madras, India
Antiseptic; 61(4):281-286 1964

Of 30,219 and 1,619 patients with proved carcinomas at Tata Memorial Hospital, Bombay and the Stanley Hospital, Madras, resp, 14,162 (85% male; 15% female; 50% of cases between 40-60 yr of age) and 642 (55% male; 45% female; 82% of cases between 40-70 yr of age) were suffering from oropharyngeal carcinoma. Leukoplakia was noted in 32% and melanoplakia in 20% of the Tata Hospital oropharyngeal cases, while poor oral hygiene was noted in 42% and 90% of the oropharyngeal cancer patients at Tata and Stanley Hospitals, resp. In the Stanley Hospital series of patients with carcinoma, the most frequent sites were: cheek, 57.6%; tongue, 13.3%, alveolus, 8.7%; palate, 6.1%; miscellaneous, 4.7%; tumors not confined to one site, 4.7%: all the lesions were squamous cell carcinoma, except for three undifferentiated carcinomas. There appears to be a correlation of oral carcinoma with poor oral hygiene, the smoking of Indian cigarettes (beedi), reversed smoking of cheroots, clay pipe smoking (lip cancer) and pan chewing; there was little correlation with race.

105. GINGIVAL CANCER.

Srivastava SP, Sharma SC
S. N. Med. Coll., Agra, U.P., India
Indian J Cancer; 5(1):89-97 1968

A combination of tobacco, lime and betel nut was chewed by 72/85 patients (age 28-80 yr) treated for gingival cancer between 1957-1965 by the department of surgery of an Indian medical college. The total group represented 1.25% of all cancer patients presenting for surgery (excluding patients with cervical, uterine and ovarian cancer); 46.73% of all cancer patients had some form of intraoral cancer. Beginning at age 31 yr, the incidence of gingival cancer increased progressively by 5-yr age groups to a peak at 46-50 yr. (27/85), then decreased progressively thereafter. Oral hygiene was poor in 80/85; 43/85 smoked cigarettes (including 37/43 who also chewed the tobacco-lime-betel nut mixture); 1/85 each had histories of giant cell sarcoma of the jaw, leukoplakia and syphilis. The male:female ratio is not indicated. The nutritional status of all patients was poor. All gingival cancers were identified histologically as squamous cell carcinomas (7/85 in Stage I, 22/85 in Stage II, 49/85 in Stage III, 7/85 in Stage IV). Lymph node metastases were seen in Stages III and IV but no remote metastases were found. The lower gum was affected in 66/85, the upper gum in 19/85.

106. REPORT OF 1,160 REGISTERED TUMOR CASES IN PAPUA AND NEW GUINEA.

Farago C
Tumor Registry Territ. Papua and New Guinea, Gen
Hosp., Port Moresby, Papua
Cancer; 16(5):670-680 1963

The author reviews 1,160 cases of malignant tumors registered between 1958-1962 in Papua and New Guinea. The incidence of registered tumors for the age group 0-9 was 7.16%; 10-19, 4.05%; 20-29, 13.97%; 30-39, 26.38%; 40-49, 27.24%; 50-59, 16.12%; over 60, 5.08%. The incidence (number of patients) of the most common forms of cancer in both sexes exclusive of primary cancer of the liver was cancer of the oral cavity, 210; skin, 189; digestive system, 133; female genitalia, 103; malignant lymphoma and leukemia, 96; and cancer of the breast (females), 52. The anatomical localization of 189 skin cancers (159 squamous cell, 11 basal cell carcinomas and 19 melanomas) was head and neck, 21; trunk, 23; upper extremities, 6; lower extremities, 100; and foot, 39. Tumors of the oral cavity had an incidence similar to that in Asiatic countries: 129/130 were betel nut chewers; smoking was common. A 14.4:1 ratio of squamous cell carcinoma to basal cell carcinoma with the localization of the former predominantly below the knee in association with chronic tropical ulcers was recorded. Tumors of the digestive tract, central nervous system and leukemia may not have been diagnosed. The incidence of lung cancer was low.

107. EPIDEMIOLOGY AND HISTOLOGY OF ORAL LEUKOPLAKIA AND LEUKOEDEMA AMONG PAPUANS AND NEW GUINEANS.

Pindborg JJ, Barmes D, Roed-Petersen B
Dept. Pub. Health, Konedobu, New Guinea
Cancer; 22(2):379-384 1968

The oral mucosa of 605 men and 621 women over 20, from 3 areas of Papua and New Guinea (179 men and 160 women from the south coast, within 30 miles of Port Moresby; 85 men and 198 women from the north coast, within 10 miles of Madang; 341 men and 263 women from the Western Highlands, within 10 miles of Mount Hagen) was examined. In these 3 areas, 76.5%, 97.6% and 74.5% of the men and 33.8%, 82.8% and 78.3% of the women, resp, were smokers; betel nut chewing was reported by 79.3%, 95.3% and 46.0% of the men and 83.8%, 95.5% and 1.9% of the women, resp. In addition to the lower prevalence of betel usage, there was a significant difference between the highlanders and coastal dwellers in the type of tobacco smoked. Nearly all of the coastal people used "tailor-made" cigarettes of "sticks" (imported tobacco wrapped in newspaper); many highlanders smoked home-cured tobacco wrapped in leaves of certain bushes, as well as tailor-made cigarettes and sticks. Betel nut chewing was an important part of the smoking habit pattern in the coastal areas, but not in the highlands. The total prevalence of leukoedema of the oral mucosa was 2.4% in the south coast (3.9% in men, 0.6% in women), 4.2% in the north coast (4.7% and 4.0%, resp) and 16.9% in the highlands (19.6% and 13.3%, resp). The prevalence of preleukoplakia in these areas was 10.6% (14% and 6.9%, resp), 12.0% (18.8% and 9.1%, resp) and 13.4% (15.8% and 10.3% resp). The leukoplakia prevalence was 6.2% (10% and 1.9%), 5.7% (7% and 5.1%) and 3.1% (3.8% and 2.3%), resp. Leukoplakia was significantly more frequent in the coastal areas than the highlands and leukoedema in the highlands; the preleukoplakia prevalence was about the same in all groups. The sex difference was significant for all diseases. No epithelial atypia, carcinoma in situ or carcinoma was noted in 26 biopsy specimens. It is suggested that smoking may be more closely associated with the risk of these conditions than previously believed.

108. REVIEW OF 110 CASES OF CANCER OF ORAL CAVITY IN PAPUA AND NEW GUINEA.

Farago C
Radiother. Dept., Port Moresby Gen. Hosp., Papua
Br Med J; 1:1264-1266 1963

On review of 110 indigenous Papuans and New Guineans receiving X-ray therapy for cancers of the oral cavity, no racial or geographical differences could be demonstrated, although all patients, with the exception of 1 male and 1 female were inveterate betel nut chewers and the majority were tobacco smokers (twist tobacco rolled in newspaper or in tobacco leaves). The constituents of the betel nut and lime chewed by the majority of patients were: fruit, leaf, root, or stem of Piper betle; Zinglber officinale: shell of Cocos nucifera; bread fruit Arthrocarpus incisa; and river shell lime. All tumors were squamous cell carcinomas, with a ratio of well differentiated: moderately differentiated:highly anaplastic of 4:2:1. The sex ratio was 3.2 males/1 female, probably due to social custom preventing women from attending hospitals. Age distribution was: 10-19, 2.7%; 20-29, 9.1%; 30-39, 29.1%; 40-49, 32.8%; 50-59, 23.6%; and 60-69, 2.7%. Distribution by site was: upper and lower lip 2.7%; tongue 27.3% (only 3/30 in females); floor of mouth, upper and lower gingiva, and hard palate, 1.8, 0.9 and 1.8%, resp, (all in males), and buccal mucosa, 65.5%.

109. CANCER PROBLEM IN BANGLADESH.

Huq SF
Dept. Radiotherapy, Dacca Medical Coll., 52/D, Azimpur Estate, Dacca 5, Bangladesh
Gann Monogr Cancer Res; 18:253-257 1976

In Bangladesh, the most common sites for cancer are the oral cavity, the laryngopharynx, the esophagus and the cervix. The high incidence of cancer of the oral cavity and laryngopharynx may be related to the habit of chewing betel-tobacco quid, and deficiencies of B vitamins and perhaps other dietary deficiencies. The high incidence of cancer of the cervix may be due to greater occurrence of injuries during childbirth and cervicitis. The high intake of red chili spice may be a factor in the rate of esophageal cancer. The frequencies of lung cancer and breast cancer are low. (1 ref)

110. CANCER OF THE ORAL CAVITY, PHARYNX/LARYNX AND LUNG IN NORTH THAILAND: CASE-CONTROL STUDY AND ANALYSIS OF CIGAR SMOKE.

Simarak S, De Jong UW, Breslow N, Dahl CJ, Ruckphaopunt K, Scheelings P, MacLennan R
Faculty Medicine, Chiang Mai Univ., Chiang Mai, Thailand
Br J Cancer; 36(1):130-140 1977

The unusually high frequency of laryngeal cancer in men (18% of all histologically diagnosed cancers) and a sex ratio of unity for lung cancer in Northern Thailand were further explored in a hospital-based case-control study in Chiang Mai. A comparison was made of patients with cancers of the oral cavity (including oropharynx), larynx, hypopharynx, and lung with controls in relation to smoking and chewing habits. Statistical analysis indicated that chewing betel is strongly associated with the occurrence of oral cancer in both sexes and with cancer of the laryngeal region in men. No factors were strongly linked to lung cancer in men, but in women, urban residence and miang (fermented wild tea leaves + salt, ginger, fried coconut, or garlic) chewing were associated with lung cancer. Analysis of smoke from the two main types of cigars smoked in the region showed that both had high tar content, but there were marked differences in pH. Smoking cigars with alkaline smoke and high tar increased the risk for laryngeal cancer in men, but smoking cigars with acid smoke and high tar together with manufactured cigarettes increased the risks for lung cancer. These increased risks were not, however, statistically significant. (21 Refs)

E. Reverse Smoking as Related to Oral Cancer

111. REVERSED SMOKING AND ITS ORAL CONSEQUENCES IN CARIBBEAN PEOPLES.

Quigley LF, Schoenfeld S, Hunt EE
Forsyth Dent. Ctr., Boston, Mass.
J Dent Res; 43(5,Suppl2):796-797 1964

The authors studied oral conditions in reversed smokers (smoking with the lighted end of a cigarette in the mouth) by means of oral biopsies, smears, and periodontal examinations. Heavy black tar deposits, leather-like tissues, heavy leukoplakia on the lips, scarring of the tongue, and reduced salivary flow were seen, along with frequent exceptionally healthy gingivae.

112. ORAL EXFOLIATIVE CYTOLOGY IN REVERSE SMOKERS HAVING CARCINOMA OF HARD PALATE.

Reddy CR, Kameswari VR
Andhra Medical Coll., Visakhapatnom, India
Acta Cytol (Baltimore); 18(3):201-204 1974

Oral exfoliative cytology was done in 165 cases of carcinoma of the hard palate occurring in reverse smokers of chuttas. All the carcinomas were proven by biopsy. Only 60% of the biopsy-proven carcinomas were cytologically positive; the other 40% showed no exfoliation of malignant cells. The normal palatine mucosa was keratinized, and more than 75% of the squamous cell carcinomas belonged to the highly differentiated grade I tumors, which probably exfoliate much less. Thus, the reliability of oral cytology in the diagnosis of palatine cancer is probably limited.

113. DISTRIBUTION OF GLANDS IN THE MUCOSA OF THE HARD PALATE AND ITS RELATION TO CARCINOMA.

Reddy CR, Venkatarathnam G, Kameswari VR
Andhra Medical Coll., Visakhapatnam-2, India
J Oral Surg; 34(3):232-236 1976

The volume of the glandular area in the mucosa of the hard palate was studied histoquantitatively in 6 fetuses and 12 adult men and women, and the results were related to the occurrence of carcinoma of the hard palate. None of the adults had been smokers or chewers of tobacco. In the fetal and adult material, neither the total area covered with glands nor the anterior extent of the glands in relation to the midline of the palate was constant. However, most of the glandular area was in the middle of the right or left half of the posterior portion of the hard palate. In the soft palate, glands were present but were located between the muscular tissue layers and in the free margin of the soft palate where there was a transition from squamous epithelium to the respiratory epithelium covering the posterosuperior aspect of the soft palate. The glandular area of the mucosa of the hard palate corresponds to the previously reported localization of carcinomas of the hard palate among women who practice reverse smoking of Indian "chuttas" (homemade cigars); this carcinoma usually occurs in the middle of the posterior half of the hard palate and not in the soft palate or in the anterior half of the hard palate. The presence of glands in the hard palate may have a role in the malignant transformation.

114. TUMORS OF THE MOUTH.

Aviles E
Departamento de Cirugia, Facultad de Medicina,
Universidad de Panama, Panama City, Panama
Rev Med Panama; 2(1):43-53 1977

The findings from 78 patients with intraoral tumors (24 benign, 54 malignant) evaluated and treated from January 1969 through December 1975 are reported. Inflammatory hyperplasia was the most commonly reported benign lesion although the torus, while being the most common, was not included because of its noninvasive nature. In the literature, the most frequent malignant intraoral tumor is adenocarcinoma of the soft palate predominantly affecting men. In this study, epidermoid carcinoma of the hard palate was the most frequently occurring malignant intraoral tumor and was found most frequently in women. Smoking with the lit end of the cigarette inside the mouth is a common habit and may contribute to the incidence of malignant intraoral tumors. (5 Refs)

115. A CORRELATIVE HISTOCYTOLOGICAL STUDY OF CARCINOMA AND EPITHELIAL ATYPIA OF THE PALATE AMONG INDIAN REVERSE SMOKERS.

Mehta FS, Sahiar BE, Daftary DK, Gupta PC, Pundborg JJ
Tata Inst. Fund. Res. Bombay, India
Br J Cancer; 26(3):230-233 1972

A correlative histocytological study was made of six patients with palatal carcinomata and 342 patients with palatal lesions (primarily leukoplakias) associated with reverse smoking from the Srikakulam district of Andhra Pradesh. Among six histologically diagnosed carcinomata only to showed cytological findings typical of carcinoma. Of the 46 atypias diagnosed histologically among the other palatal lesions, only six (13%) were diagnosed cytologically. Findings show that cytological examination of precancerous and cancerous lesions located on the hard palate, which is a highly keratinized area of the oral cavity, may not be reliable enough for revealing premalignant or malignant changes.

116. EPIDERMOID CARCINOMA OF THE PALATE. HOSPITAL SANTO TOMAS 1969-1973.

Young K, Hernandez L
Centro Oncologico J. D. Arosemena, Lima, Peru
Rev Med Caja Nac Soc; 8(2):246-247 1976

Epidermoid carcinoma of the palate in Lima, Peru, is attributed to the custom, especially among women, of smoking cigarettes with the lit end inside the oral cavity. In a 4 yr period, 68 cases of palatine epidermoid carcinoma were studied. Palatine epidermoid carcinoma can be treated effectively with radiotherapy or surgery. (1 Ref)

117. REVERSE DHUMTI SMOKING IN GOA: AN EPIDEMIOLOGIC STUDY OF 5,449 VILLAGERS FOR ORAL PRECANCEROUS LESIONS.

Bhonsle RB, Murti PR, Gupta PC, Mehta FS
Basic Dental Res. Unit, Tata Inst. Fundamental Res.,
Homi Bhabha Road, Bombay-400 005, India
Indian J Cancer; 13(4):301-305 1976

The prevalence of tobacco habits, with particular emphasis on reverse dhumti smoking and its association with oral cancer and precancerous lesions, was studied in Goa. Dhumti is made by rolling a tobacco leaf inside the leaf of a jackfruit tree; males smoke in the conventional manner but females may also smoke it in a reverse manner keeping the burning end inside the mouth. Using random sampling, 5,449 individuals in 11 villages were examined by dentists in a house-to-house survey. Reverse dhumti smoking was practiced by 0.4% of the sample. Leukoplakia was found in 1.6% of the population, leukokeratosis nicotina palati in 1%, lichen planus in 0.2% and submucous fibrosis in 0.04%. A correlation of various lesions with tobacco habits is tabulated. A marked association was observed between palatal lesions and the habit of reverse dhumti smoking practiced exclusively among Christian females in this study. Among 24 reverse dhumti smokers, 25% had leukokeratosis nicotina palati. The association of other tobacco habits with oral lesions was similar to that reported from other parts of India. (8 Refs)

118. INTERNATIONAL CONFERENCE ON THE EPIDEMIOLOGY AND PATHOLOGY OF ORO-PHARYNGEAL TUMORS.

Nugmanov SN
Kazakhstan Inst. Oncol. Radiol., Alma-Ata, USSR
Vopr Onkol; 10(7):123-124 1964

The participants of a WHO-sponsored conference in New Delhi, in October, 1963, reported on the epidemiology of oropharyngeal tumors. In India they comprise 50% of all malignancies and are attributed to smoking, anemia, avitaminosis, etc. Cancer of the palate is more frequent here in females who practice inverted smoking. Experiments indicate that cigarette smoke is only an early contributing factor; heat actually favors the process of carcinogenesis. In South Africa tumors of the oral cavity are more frequent in males, and they occur without predilection for white or native population. In Japan gastric cancer is attributed to salty foods and insufficient milk consumption; the mortality is higher in females of low socioeconomic classes. Overall, the rate of gastric cancer among various races depends on their eating habits.

II. CANCER OF THE ESOPHAGUS

EDITOR'S NOTE: Section VII lists comparative epidemiological studies dealing with multiple cancer sites, including the esophagus. Additional studies, dealing with both esophageal and oral cancer, may be found in the preceding section, "Cancer of the Oral Cavity."

A. Epidemiological Studies, Including the Role of Alcohol, Diet, and Smoking in Esophageal Cancer

119. EPIDEMIOLOGY OF ESOPHAGEAL CANCER.

Haas JF, Schottenfeld D
Cornell Univ. Medical Coll., New York, NY, 10021
Gastrointest Tract Cancer; 145-172 1978

The geographical pathology, demographic characteristics, and etiology of esophageal cancer (EC) are reviewed. Dramatically different patterns of occurrence are observed for EC in different parts of the world, among different ethnic groups, and in men and women. There is no unifying hypothesis to explain the varied epidemiological picture presented by EC in different regions of the world. This picture suggests that there is more than one environmental determinant. Alcohol apparently plays a role in the development of EC, particularly in North America and Europe, although there is no evidence that it acts directly as a carcinogen. Tobacco smoking, closely tied with alcohol consumption, seems to make an independent contribution to EC. Smoking induces dose-related histological changes in the esophageal squamous epithelium that are strongly reminiscent of those preceding bronchogenic carcinoma. In areas such as the Caspian littoral, where EC is not tobacco- or alcohol-related, dietary factors are of special concern. Geophysical environment may be reflected in the effect of local soil characteristics on diet. Molds productive of carcinogens could be geographically limited food contaminants. Mucosa conditioned by chronic specific nutritional deficiency may be especially vulnerable to the action of carcinogens. (106 Refs)

120. CARCINOMA OF THE ESOPHAGUS.

Postlethwait RW
Surgical Service, Durham Veterans Admin. Hosp., Durham, NC
Curr Probl Cancer; 2(8):1-44 1978

Cancer of the esophagus is reviewed. Approx 98-99% of malignant tumors of the esophagus are squamous cell carcinomas. The incidence of esophageal cancer is high in the Gonbad area in Iran, the Transkei in South Africa, the Honan province in China, in Turkmenia in the USSR, and in Rhodesia. The high incidence in these areas suggests that a predisposing factor, such as diet or habits of alcohol or tobacco use, may play a role in the etiology of this malignancy. Most esophageal cancers (63.6%) occur in the age range of 50-60 yr. Diagnosis is seldom difficult but the aggressive nature of the disease, with invasion or metastases occurring relatively early, makes effective treatment difficult. The pathology, diagnosis, selection of treatment, preoperative care, resection, postoperative care, postoperative morbidity and mortality, irradiation and chemotherapy, palliative treatment, and the results of surgical treatment are discussed. Only 30% of esophageal carcinomas are resectable and the 5-yr survival of all patients is in the range of 3%. Other malignant tumors of the esophagus (adenocarcinoma, leiomyosarcoma, melanoma, carcinosarcoma, pseudosarcoma) and benign tumors and cysts are briefly considered. (47 Refs)

121. CERTAIN MORTALITY PATTERNS OF ESOPHAGEAL CANCER IN THE UNITED STATES, 1930-67.

Schoenberg BS, Bailar JC, Fraumeni JF
Biometry and Epidemiology Branches, NCI, Bethesda, MD, 20014
J Natl Cancer Inst; 46(1):63-73 1971

Cancer of the esophagus shows substantial racial, geographic, and temporal variations within the United States. In a cohort analysis of mortality during 1930-67, the nonwhite population experienced steadily and rapidly increasing rates, while those of the white population remained relatively stable. The rising nonwhite mortality occurred at all ages and all areas of the country and was more pronounced among males than females. Death rates in the Northeast were consistently higher than in other regions of the country, with the geographic differential being more prominent among nonwhites (threefold) than among whites (twofold). Detailed analysis of the nonwhite statistic for 1950-66 showed that Negro males and females, together with Chinese and Japanese males, contributed to the excess in mortality. However, only Negroes had a steady increase in mortality over time. To study factors implicated in the origin of esophageal cancer, mortality rates by States for 1950-66 were compared with the following variables for each State: the percentage of population living in urban areas, per capita cigarette sales, and per capita alcohol sales. Mortality showed significant geographic corelations with each of these 3 variables, but the associations with cigarette and alcohol consumption seemed to result from some other, still unidentified, hazard in the urban environment. The striking racial variatons in esophageal cancer suggest that Negroes have been increasingly exposed, and are more susceptible, to these carcinogenic influences. (Author abstract) (26 Refs)

122. THE OCCURRENCE OF OESOPHAGEAL CANCER - A WORLD-WIDE SURVEY (MEETING ABSTRACT). (P. 20)

Muir CS
International Agency Res. Cancer, Lyon, France
National Cancer Week, Proceedings of the Australian Symposium on Nutrition and Cancer held in Adelaide, Australia, 20-24 November 1978. South Australian Postgraduate Medical Education Association Incorporated, 175 pp., 1978.

The geographical distribution of esophageal cancer shows an extraordinarily large variation - possibly greater than for any other cancer site. There appears to be a high risk belt extending across Central Asia from Eastern Turkey to Northern China. In some areas of Africa, Europe and Asia, significant differences can be observed over relatively small distances. Morbidity data published in Cancer Incidence in Five Continents supplemented by material collated by other investigators are presented. The highest recorded age-adjusted rates for both sexes are those from Northern Gonbad (Iran), respectively 93.1 and 110.0/100,000/yr for males and females. Sex ratios vary independently of incidence level, ranging from 29.0 for Africans of Bulawayo to 0.9 in the Indian population of Singapore and 0.7 in Langarud (Iran). For esophageal cancer, mortality can be considered to be a fair approximation of morbidity; available data are given. For the several areas of the world for which neither morbidity nor mortality data are available, relative frequency ratios are discussed. Risk is increased by heavy alcohol consumption and the use of cigarettes (both independently and in a multiplicative manner), home-brewed beers, tarry tobacco residues which are scraped from pipes then eaten, a diet low in animal fat and riboflavin, the tarry residues from opium pipes, chewing betal quid concomitently with tobacco smoking, and various dietary factors. (no Refs)

123. EPIDEMIOLOGY OF ESOPHAGEAL CARCINOMA (LETTER TO EDITOR).

Mizroch S
Kaiser Foundation Hosp., San Francisco, CA
JAMA; 239(22):2340-2341 1978

Age (older), sex (male), race (nonwhite), and geography exert substantial influence on the increased incidence of esophageal carcinoma. Cigarette smoking, alcohol consumption, and thermal irritation from imbibing hot foods are also predisposing factors. There are links between carcinoma and various types of obstructive esophageal lesions. An increased incidence of carcinoma in achalasia, Barrett's esophagus, lye strictures, and Plummer-Vinson syndrome should encourage the high index of suspicion incumbent to early diagnosis.

124. COMPARISON OF ESOPHAGEAL CARCINOMA IN THE AMERICAS, ASIA AND AFRICA (MEETING ABSTRACT).

Burdette WJ
Univ. Texas Medical Sch., Houston, TX
Proc Am Assoc Cancer Res; 15:190 1974

After 1805 cases and /or specimens of epidermoid carcinoma of the esophagus were reviewed in Houston, Zaire, Johannesburg, the Transkei, Brazil, Colombia, Lima, Santiago, La Plata, Buenos Aires, Curacao, and the People's Republic of China, a comparison of the natural history of the disease, occupation, age at onset, gross appearance, and microscopic variations were remarkably similar in all locations, with extensive disease presenting as a problem of dysphagia. The location and sex ratio (1.4-9.4) were not constant. Smoking and drinking alcohol were commonly but not invariably associated with the disease, and multiple etiologies are obviously involved. One patient was trisomic for chromosome 21. Prevalence varied with race and geography. The results of treatment suggest that immediate bypass with colon or reversed gastric tube and subsequent excision is a logical means for improving palliation and survival, with better results in cervical than thoracic lesions. Combined therapy requires cooperative clinical trials for evolution of satisfactory method(s). There is suggestive evidence that screening with exfoliative smears in high-risk populations will yield more curable cases.

125. THE OESOPHAGEAL CARCINOMA PROBLEM IN TRANSKEI: A GEOGRAPHIC REAPPRAISAL.

McGlashan ND
Dept. Geography, Univ. Tasmania, Hobart 7001, Australia
S Afr J Sci; 73(10):294-299 1977

A geographic plot of the home districts of 79 Transkei miners, who were returned to their homes because of esophageal cancer and of the home districts of 1,554 Transkei residents with the same cancer reveals a remarkable overlap in the regions of highest incidence. Cancer incidence increases as one goes from northeast to southwest. The etiological agent responsible for this cancer is apparently social rather than physical, because the physical environment variation is on an axis at right angles to that of the disease (the 2 axes oppose each other). The pattern of primary liver cancer is similar to that of esophageal cancer. It is postulated that varying degrees of exposure to the same carcinogen could account for both these cancers. Because of the noticeable demarcation between areas of high and low incidence, study of only a few high- and low-risk areas should provide sufficient etiologic data. Nitrosamines, mycotoxins (aflatoxins), and tobacco merit investigation as possible etiologic agents. (21 Refs)

126. SMOKING AND CANCER OF THE ALIMENTARY TRACT IN POLAND.

Staszewski J
Inst. Oncol., Gliwice, Poland
Br J Cancer; 23(2):247-253 1969

A retrospective study was made during 1957-59 and 1960-68 of 81 males and 7 females with carcinoma of the esophagus, 450 males and 178 females with carcinoma of the stomach and 240 males and 198 females with carcinoma of the large bowel. Controls were 771 males and 383 females hospitalized with disorders thought not to be associated with smoking habits. In males with carcinoma of the esophagus and stomach there was a significantly higher tobacco consumption than in controls. Results in females did not differ significantly from controls. For males, relative risk of male smokers vs nonsmokers for carcinoma of the stomach was 1:6. When carcinoma of the stomach was classified by location in the stomach, male patients with carcinoma of the cardia and carcinoma of the pyloric region had significantly higher smoking indices while patients with carcinoma of the middle portion or whole of the stomach did not differ significantly from controls in their smoking habits. Females with carcinoma of the cardia also differed significantly from controls in having a higher tobacco consumption.

127. MORTALITY IN RELATION TO SMOKING: TEN YEARS' OBSERVATION OF BRITISH DOCTORS.

Doll R, Hill AB
Coll. Hosp. Sch. Med., U. London
Br Med J; 1:1399-1410 1964

Survivors of a survey of smoking habits of British doctors conducted in 1951 were sent second questionnaires in 1958, and calculated standardized mortality rates in relation to smoking for all ages were obtained. Total deaths include 4,597 men and 366 women. Among male doctors, a steadily rising death rate (per 1,000) was seen for lung cancer mortality with increasing consumption of cigarettes at every age above 45 yr. For each type of smoking (cigarettes alone, mixed, pipe and/or cigars alone) the lung cancer death rate in continuous smokers was higher than that of those who had stopped, while the rate in ex-cigarette smokers (0.24) was notably less than that in current pipe smokers ((0.47). Lung cancer death rate for those who had given up smoking was 19% lower than the rate for continuing smokers. According to histologic type mortality ratios (with standard death rate of continuing cigarette smokers = 100%) for those smoking 1-14, 15-24 and 25 or more cigarettes/day, resp, in those in the squamous group was 68%, 104%, and 139%; in the oat cell and anaplastic group 44%, 91% and 169%. Of deaths from other cancers considered (oropharynx, nose, larynx, esophagus), only cancer of the esophagus shows a progressive increase in mortality with increased smoking and a marked reduction in those who have stopped. In men who have given up smoking, mortality rates from lung cancer were found to decline immediately and became progressively smaller as the length of time increased since smoking had been given up. While mortality from all causes was slightly higher in inhalers (17.73) than in non-inhalers (15.83), the largest relative excess was observed with lung cancer (71%). Among women doctors, total mortality among cigarette smokers was identical with that among nonsmokers. Lung cancer mortality was highest among women who smoked 15 or more cigarettes a day. The age at which smoking started and different inhaling habits were found to be influencing factors.

128. THE EPIDEMIOLOGY OF CANCER OF THE OESOPHAGUS.

Cook-Mozaffari P
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Nutr Cancer; 1(2):51-60 1979

The epidemiology of esophageal cancer (EC) is reviewed. The range of incidence between different regions varies 500-fold. Sharp gradients of incidence occur between regions only a few hundred miles apart. High-incidence areas (HIA's) have been found in Iran and in southern and eastern Africa. Sometimes the rates for women show the same high frequency as those for men, but often they occur at a much lower level. In the HIA's of Normandy and Brittany, the male:female ratio is greater than 25:1. Clear but small-scale increases in incidence have been recorded for both sexes among US Blacks and for men in northern France. During the last 30-40 yr, EC has become one of the commonest types of cancer diagnosed in southern Africa; previously, it was nonexistent. In the HIA of Iran, however, the disease was described as long ago as the 12th century. In several HIA's vitamin A and riboflavin deficiencies appear to be associated with EC. In Kenya and other parts of Africa, there is some evidence to implicate home-brewed beer made from maize. A case-control study in Normandy and Brittany indicated that most of the excess risk for EC could be ascribed to a multiplicative effect of drinking and smoking. However, the sum of these various factors is not sufficient to account for the exceptionally high incidences and extraordinary pattern of variation of EC. (59 Refs)

129. CARCINOMA OF THE OESOPHAGUS IN THE SUDAN.

Boulos PB, El Masri SH
Dept. of Surgery, Univ. of Khartoum, Sudan
Trop Geogr Med; 29(2):150-154 1977

The incidence of cancer of the esophagus in the Sudan was investigated. Histopathological reports of 135 cases of this cancer were examined and clinical data from 14 of the cases were analyzed. In the Sudan, cancer of the esophagus accounted for 1.4% of all malignant tumors. The disease affected both sexes equally, and more than one-half of the occurrences were in patients between 50 and 60 yr of age. The cancer was much more prevalent in patients from the North. While relation between the incidence of tumors and alcohol consumption was noted, the use of tobacco under the tongue or in the labiodental groove has been implicated in oral cancer and may play the same role in this cancer. Iron deficiency has also been implicated in lesions of the upper esophagus. However, despite the high frequency of iron anemia in the Sudan, cancers at this site were not more prevalent than at other sites. A very low resection rate was due to the poor condition of the patients when seen. Treatment usually consisted of radiotherapy or palliation. (27 Refs)

130. CANCER OF THE ESOPHAGUS IN DJIBOUTI. REPORT OF 36 CASES COLLECTED IN TWO YEARS.

Gendron Y, Ardouin C, Lassalle Y, Sirol J
Hopitaux des Armees, Djibouti, French Somaliland, E. Africa
Bull Soc Pathol Exot; 70(1):74-82 1977

In an African hospital, 36 patients (29 men, 7 women aged 40-70 yr) with cancer of the esophagus were observed within a 2-yr period. Clinical symptoms included dysphagia, regurgitation, and pain, and diagnosis was established by radiography in all patients and biopsy specimens obtained by fibroscopy in 24. Only palliative therapy was attempted, since the cancers were well advanced, and they coexisted with hepatomegaly and/or subclavicular adenopathy in 14 patients. The patients were all African orientals who chewed the leaf of the Khat shrub, which was suspected as being the etiological factor because the active principle of the plant is an alkaloid. Esophageal endoscopic examination of 50 patients (aged 20-40 yr) with duodenal ulcers who chewed 100-300 g of Khat daily revealed a nonspecific inflammation in only 2. Examination of 30 men (aged 30-60 yr) who consumed larger quantities, 200-500 g/day over a 15-yr period and who smoked 20-40 cigarettes/day revealed only 1 case of esophagitis. Khat cannot be ruled out as an etiological factor, since the number in this series was small. Genetic factors may be predisposing to esophageal cancer, as it is prevalent only among the various ethnic populations who habitually chew Khat. (12 Refs)

131. AN EPIDEMIOLOGICAL STUDY OF ESOPHAGEAL CARCINOMA IN OKLAHOMA CITY HOSPITALS, 1970-1975 (MEETING ABSTRACT).

Kenya PR, Asal NR
Univ. Oklahoma, Oklahoma City, OK 73190
Am J Epidemiol; 106(3):240 1977

A retrospective investigation comparing associated risk factors in 181 newly diagnosed cases and a matched group of controls obtained from hospital records and a mailed questionnaire was carried out with the main objective of exploring the independent roles of alcohol and tobacco consumption in the etiology of esophageal carcinoma. Several factors were found to be associated with esophageal carcinoma. Some of these factors include a history of regular exposure to chemicals, toothlessness without prosthetic replacement, family history of esophageal cancer, family history of gastrointestinal cancer and family history of cancer. Both smoking and alcohol consumption were found to be associated with esophageal cancer. The association was stronger for smoking than for alcohol. Among nonsmokers, alcohol was not found to be associated with the disease. However, in the presence of alcohol the risk of developing esophageal cancer increased in smokers. The amount of tobacco and/or alcohol used was very important in determining the strength of the association. Heavy smokers who were heavy drinkers had a relative risk value of 10.52. The importance of controlling alcohol and smoking use independently and in combination when testing for the relationship of esophageal carcinoma and a suspected attribute will be discussed. (Author abstract) (no Refs)

132. FACTORS ASSOCIATED WITH CANCER OF THE ESOPHAGUS, MOUTH, AND PHARYNX IN PUERTO RICO.

Martinez I
Cent. Cancer Registry, San Juan, Puerto Rico
J Natl Cancer Inst; 42(6):1069-1094 1969

A case-controlled, community-based study was made of 400 patients with epidermoid carcinoma of the esophagus, mouth and pharynx diagnosed in all hospitals and clinics in Puerto Rico during 1966. Each patient was matched with 3 controls, one from the same hospital or clinic and 2 residents of the same community for at least 10 yr. Among the 400 lesions, 179 were in the esophagus (120 in males, 59 in females) with 52% of them in the middle third of this organ, 153 were in the mouth (115 in males, 38 in females) with 40% and 50% in the tongue of males and females, resp and 68 were in the pharynx (55 in males, 13 in females), with 45% in the hypopharynx. Overall male-female ratio was 2.6:1. The patients with epidermoid carcinoma differed significantly from controls in their higher consumption of alcohol, tobacco, hot beverages (mostly coffee) and spices. They also had more irregular eating patterns, had fewer meals per day and a smaller amount of food per meal, which was consumed while very hot and without beverage. The incidence of cancer of the esophagus in Puerto Rico is among the highest in the world; cancer of the mouth and esophagus is also high.

133. EPIDEMIOLOGY OF ESOPHAGEAL CANCER IN THE AKTIUBINSK REGION OF KAZAKH SSR.

Bashirov MS, Nugmanov SN, Kolycheva Vop NI
Kazakh Sci. Res. Inst. Cancer Rad., U.S.S.R.
Vopr Onkol; 14(8):3-6 1968

Esophageal cancer morbidity in the Aktiubinsk region in 1965 was 46.49/100,000 population, or 30.1% of all other cancer forms; from 1959-1965, 1426 cases were registered, of whom 1314 (92.14%) were Kazakhs. In 1959, the morbidity rate/100,000 was 75.6 and only 6.6 in Russians in the same territory. These 1426 patients included 719 males and 707 females; the 1965 morbidity rates were 43.5 and 49.7/100,000, resp. Among 301 cancer patients (142 males, 159 females) used for epidemiological studies, 94.35% of the patients and 96.34% of controls were born and lived in the Aktiubinsk region; 10.3% and 5.3% resp, had family histories of esophageal cancer. Consumption of hot tea was high in 129/142 males and 158/159 females with cancer (over 6 cups at a time; over 10 cups at a time in 40.22% males and 45.25% females), compared to 113/142 male and 156/159 female controls (41.55% and 69.18%, resp, with very high tea consumption). Therefore, hot tea could not be considered a basic factor causing the increase in the esophageal cancer frequency among Kazakhs. However, 43.66% of the male cancer patients and 21.12% of the male controls drank tea in a reclining position (all females drank tea while seated). A possible connection is discussed. Among male patients 38.73% were smokers (72.72% of them for 21 yr, or more compared to 19.7% and 78.6%, resp, in controls. Among females, 3.7% of the patients were smokers, compared to 0.6% of controls. Therefore, smoking had no essential role in the development of esophageal cancer. The use of "nas" (a preparation containing Nicotiana rustica) was reported in 23.24% and 1.88% of the male and female cancer patients, resp, compared to 30.98% and 1.26%, resp, in controls. Alcohol consumption was found among 57.74% of the male cancer patients (9 showed alcohol abuse) and 44.3% of the controls. Females of both groups denied alcohol consumption. Therefore, alcohol plays no role in the development of esophageal cancer. Histories of esophagitis and injuries were noted in 7/301 and 10/301 with cancer, resp.

134. CANCER IN THE NATAL AFRICAN, 1964-66. CANCER MORBIDITY INCIDENCE AND GEOGRAPHICAL PATHOLOGY IN THE NATAL HINTERLAND.

Schonland M, Bradshaw E
U. Natal, Durban, South Africa
S Afr J Med Sci; 33(2):33-42 1968

Cancer morbidity rates from 1964-1966 were studied in the African population (predominantly Zulus) of 2 urban (Durban and Pietermaritzburg) and 4 rural areas of Natal. Of the 3174 new cancer cases seen in the hinterlands, 1673 were in males and 1501 in females (standardized morbidity 57.7 and 45.8, resp). Crude cancer morbidity rates for the Natal hinterlands were about 50% of the rates in Durban (139.0 in males, 120.7 in females) and Pietermaritzburg (128.7 and 105.8, resp); this was attributed to the limited diagnostic and therapeutic services for Africans living in the hinterlands, particularly in the remote reservation districts. In general, the districts associated with opportunities for cash wage earnings in the towns showed a relatively high incidence of lung and esophagus cancer (attributed to cigarette smoking and alcohol consumption) and a decreased incidence of cervix cancer (attributed to better hygienic standards and socioeconomic conditions). Cancer of the cervix and skin (excluding Kaposi's sarcoma), musculoskeletal tumors, leukemia and lymphoma were more frequent in the remote districts where living conditions were poor, the av socioeconomic status was low and water was very scarce. Variations in the cancer incidence among the subdivisions of the Natal hinterland were attributed to differences in available diagnostic services.

135. SMOKING, DRINKING AND OESOPHAGEAL CANCER IN AFRICAN MALES OF JOHANNESBURG, SOUTH AFRICA.

Bradshaw E, Schonland M
South African Inst. Med. Res., Johannesburg
Br J Cancer; 30(2):157-163 1974

A study of the smoking and drinking habits of 196 esophageal cancer cases and 1064 control patients was made. All subjects were African males aged 35 yr or more, drawn from a mainly urbanized population. It was found that tobacco smoking was prevalent and that pipe tobacco (used in pipes or in hand rolled cigarettes) was used more frequently than has been found in westernized countries. The drinking of alcohol was also a prevalent habit. Tribal affiliations were examined and all three of these factors showed differences between cases and controls. Further analysis of smoking and drinking together showed that only smoking had a positive association with esophageal cancer, and this was also true after tribal adjustment had been made. A comparable analysis of data on Durban African males yielded similar findings. It is concluded that tobacco smoking was a powerful esophageal insult but it was not shown that alcohol was important in the development of esophageal cancer. Cigarette tobacco does not appear to be a significant esophageal insult but pipe tobacco does, and the use of both these types of tobacco together may have a synergistic effect. Tribal affiliation has bearing on the smoking pattern.

136. OESOPHAGEAL AND LUNG CANCERS IN NATAL AFRICAN MALES IN RELATION TO CERTAIN SOCIOECONOMIC FACTORS. AN ANALYSIS OF 484 INTERVIEWS.

Bradshaw E, Schonland M
U. Natal Cancer Survey Unit, Durban, South Africa
Br J Cancer; 23(2):275-284 1969

A study of 484 African males interviewed at a large Durban hospital from 1964-1966 included 98 cases of esophageal cancer, 45 cases of lung cancer and 341 cases of nonmalignant diseases. The cancer group differed significantly from the control group in 4 variables: (1) They used emetics regularly and purgatives frequently, with most of the medicaments being provided by herbalists and witch doctors. It is uncertain what relation these remedies have with onset of cancer. (2) The drinking of local alcoholic concoctions was higher in cancer groups, and patients with lung cancer consumed more concoctions than those with esophageal cancer. (3) There were more tobacco smokers in the cancer groups than in the controls. Esophageal cancer patients tended to smoke pipes, and lung cancer patients smoked cigarettes. Both cancer groups had an excess of males who have smoked for 30 yr or more as compared with the controls. Both cancer groups smoked more tobacco than the controls; the esophageal group had the highest lifetime consumption, but 15% of the esophageal group never smoked. (4) More cancer patients were exposed to 1 or more occupational carcinogens than controls. These included petrol/oil and tar/pitch in lung cancer, and lead, asbestos and possibly soot in esophageal cancer. Specific carcinogens were not determined.

137. REGIONAL AND SOCIAL DIFFERENCES IN CANCER INCIDENCE OF THE DIGESTIVE TRACT IN THE GERMAN DEMOCRATIC REPUBLIC.

Berndt H, Wildner GP, Klein K
Cancer Res. Inst. , German Acad. Sci., Berlin
Neoplasma; 15(5):501-515 1968

A significant correlation between population density and the age-adjusted incidence of all cancers combined (1959) was found in East Germany. The age-adjusted incidence of stomach cancer declined from 1960 to 1965; it was lower in the central portion of East Germany (including Berlin) than in the northern (predominantly rural) and some of the southern (predominantly urban-industrial) regions. This regional variation could not be explained. Cancer of the esophagus was more frequent in the northern regions than in the southern regions; the highest incidence was seen in Berlin. The most important etiologic factors for this tumor were alcohol consumption and smoking. The incidence of cancer of the colon in East Germany increased from 1960 to 1965. This tumor was far less frequent in the northern and central regions than in Saxony, Thuringia, Berlin and Leipzig. A correlation between the incidence of this cancer and high socioeconomic status was noted; cigar smoking is suggested as an etiologic factor. Cancer of the rectum was less frequent in the northern areas than in the central and southern areas, but the correlation between the incidence of this cancer and urbanization was not significant. This geographical variation could not be explained.

138. EPIDEMIOLOGY OF CANCER OF THE ESOPHAGUS.

Takano K, Osogoshi K, Kamimura N, Kanda K, Kane K, Kamiyama R, Sakamoto K, Sato H, Shirai Y, Sei M, Tanabe T, Horino M, Minami Y, Motoji H, Morita R, Orihata H, Hirayama T
Women's Med. Coll., Tokyo
Jpn J Clin Med; 26(8):1823-1828 1968

The relative risks of esophagus cancer were studied in a small group of cancer patients (167 men, 33 women) and the same number of normal subjects. The relative risk was higher in rural residents than in urban residents; this was attributed to poor nutrition (diets consisting mostly of soy soup, rice and noodles) in the rural areas; persons reporting a high consumption of bread, fruit and milk showed a low relative risk. Other factors associated with a high relative risk of esophagus cancer were the consumption of hot foods, daily consumption of liquor (especially sake) and heavy smoking (more than 20 cigarettes /day), particularly in persons reporting all 3 habits combined. The relative risk associated with smoking alone was increased only slightly.

139. OESOPHAGEAL CANCER AND ALCOHOL CONSUMPTION: IMPORTANCE OF TYPE OF BEVERAGE.

Tuyns AJ, Pequignot G, Abbatucci JS
International Agency Res. Cancer, 150 Cours Albert Thomas, 69372 Lyon Cedex 2, France
Int J Cancer; 23(4):443-447 1979

The role of alcohol consumption in esophageal cancer in Normandy, France, was assessed by a retrospective study of 312 male patients and 869 age-matched controls. The linear relationship between the logarithm of risk and overall daily alcohol consumption was confirmed after adjustment for tobacco. The role of each specific alcoholic beverage was further investigated by computing relative risks for individuals consuming a given beverage and for those drinking other beverages only, within each overall alcohol consumption category. It was concluded: (1) that there is a linear relationship between the logarithm of risk of esophageal cancer and overall daily ethanol consumption, whatever the beverage; (2) that the effect is more marked for strong beverages (ie, liqueurs, brandies) than for lighter beverages; and (3) that there is an additional risk related to apple brandy and cider. One possible reason for the extra risk related to cider and its distillates might be the presence of carcinogens in these beverages. (13 Refs)

140. CANCER OF THE OESOPHAGUS: FURTHER EVIDENCE OF THE RELATION TO DRINKING HABITS IN FRANCE.

Tuyns AJ
Int. Agency Res. Cancer, Lyons, France
Int J Cancer; 5(1):152-156 1970

Age-specific annual mortality rates (1960-1963) for esophageal cancer, alcoholism and liver cirrhosis, in males aged 46-64 yr, were analyzed for the 88 departments and 21 regions of France. Significant positive correlations were found between esophageal cancer and alcoholism and between esophageal cancer and cirrhosis. All of the departments showing cancer mortality rates of 50/100,000 or more also showed alcoholism mortality rates of at least 70/100,000; these departments were all in western France. In Haute-Savoie, Savoie and Ardennes, however, the cancer mortality rates were "normal" (30-40/100,000) while the alcoholism mortality rates were high. Since acute or chronic alcoholism (related to distilled liquors) showed a higher correlation with cancer of the esophagus than did liver cirrhosis (related to wine or beer), it is suggested that the carcinogen(s) responsible for this tumor may require conc alcohol as a vehicle. It is also suggested that the carcinogen(s) may be present in liquors consumed in some areas of France (notably western France) but not in other areas such as Savoie.

141. CANCER OF THE OESOPHAGUS IN BRITTANY: AN INCIDENCE STUDY IN ILLE-ET-VILAINE.

Tuyns AJ, Masse G
Int. Agency Res. Cancer, Lyon, France
Int J Epidemiol; 4(1):55-59 1975

A morbidity survey was initiated to confirm the findings of high mortality from esophageal cancer in Brittany and Normandy. A registry, limited to esophageal cancers observed in the department of Ille-et-Vilaine was established in Rennes. Information was collected from the Regional Cancer Center, departments of pathology and ENT surgery, Social Security files, death certificates, and regional and local hospitals. An accurate tabulation of cases was complicated by repeated reporting. From 1968-1973, 718 cases were entered, 699 males and 49 females. Crude incidence rates were 35:8 and 2:4, resp. and corresponding age-standardized rates were 29:4 and 1:2, resp./100,000 population. The figures for females were within ranges observed elsewhere in Europe and were not examined further. Forty percent of the tumors occurred in the middle third of the esophagus, 26% in the lower third, 9% stretched over both, 15% in the upper third, and 8% were stretched over the upper and middle thirds. Eighty percent of the tumors examined were squamous cell carcinomas; 7% were adenocarcinomas. There was a high endemicity in the rural areas north of Ille-et-Vilaine with rates reaching 60/100,000. It is suggested that the high incidence of esophageal cancer is related to various etiological factors such as the consumption of local brands of apple cider distillants. Dietary, smoking, and drinking habits in relation to esophageal cancer are now being investigated.

142. ESOPHAGEAL CANCER IN ILLE-ET-VILAINE, FRANCE, IN RELATION TO ALCOHOL AND TOBACCO CONSUMPTION: MULTIPLICATIVE RISKS.

Tuyns AJ, Pequignot G, Jensen OM
International Agency Res. Cancer, 150, cours Albert-Thomas, F 69008, Lyon Cedex 2, France
Bull Cancer (Paris): 64(1):45-60 1977

A retrospective case-control study of 200 men with esophageal cancer and 778 population controls was carried out in Ille-et-Vilaine, France. The logarithms of the relative risks of developing the disease increase linearly with daily consumption of alcohol or tobacco. The combined effects of both fit with a multiplicative model that is proposed. This model could be applicable to other situations. It explains the sex ratio and the urban/rural differences observed in Ille-et-Vilaine. The practical implications for public health purposes are discussed briefly. (22 Refs)

143. ALCOHOL AND OESOPHAGEAL CANCER: AN ASSESSMENT OF THE EVIDENCE FROM ROUTINELY COLLECTED DATA.

Chilvers C, Fraser P, Beral V
Epidemiological Monitoring Unit, London Sch. Hygiene and Tropical Medicine, London, England
J Epidemiol Commun Health; 33(2):127-133 1979

Mortality and morbidity due to esophageal cancer in England and Wales were investigated. The mortality rate declined after 1911, then increased during the 1950's in all except the oldest age groups. The generation of males born in 1906 had a lower mortality than any preceding or succeeding generation. Morbidity rates increased 52% among males and 54% among females during the period 1962-63 to 1973-74. Since 1900, there was a steady decline in the consumption of alcohol until after World War II, when consumption increased. Consumption of beer contributed to total alcohol consumption. For both males and females, cohort mortality was closely correlated with the per capita consumption of total alcohol when the cohort was aged 25-29 yr (p less than 0.01). Cigarette smoking has increased steadily since 1905 except for a sharp decline between 1946 and 1950. There was no relationship between cigarette consumption in different generations and mortality from esophageal cancer. Mortality from cirrhosis of the liver and esophageal cancer was highly correlated on a regional basis among males (p less than 0.1) but not among females. Internationally, for males, but not females, there was also an association between total alcohol consumption and esophageal cancer (p less than 0.01); there was a weaker association with wine (p less than 0.05) but not beer or spirit consumption. The international data suggest that ethyl alcohol itself rather than any specific alcoholic beverage is associated with esophageal cancer. (29 Refs)

144. NEGLIGIBLE ROLE OF ALCOHOL AND TOBACCO IN THE ETIOLOGY OF ESOPHAGEAL CANCER IN IRAN - A CASE CONTROL STUDY. (PP. 1149-1159)

Mahboubi E, Day NE, Ghadirian P, Salmasizadeh S
Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, Omaha, NB
Third International Symposium on the Detection and Prevention of Cancer held by the International Study Group for the Prevention and Detection of Cancer in New York, April 26-May 1, 1976. Part I, International Study Group for the Prevention and Detection of Cancer New York, NY, Vol. 1, 1193 pp., 1977.

A case-control study was conducted to determine the influence of alcohol, tobacco, and opium use on esophageal cancer (EC) in an area with a high EC incidence, the Caspian Littoral of Iran. In interviews with 151 patients and 301 healthy controls, alcohol consumption and smoking were found to be neglible. Regular opium use appeared to increase the cancer risk, but the possibility of bias in responses could not be excluded. It is suggested that the long-term nutritional deficiencies that exist in this region may be related to the increased risk of EC, without the added influence of tobacco or alcohol. These deficiencies are particularly severe among Turkomans. Since the present study failed to pinpoint any specific factor or known carcinogen, the combination and/or interaction of several factors may be involved in the etiology of EC. These factors include nutritional deficiency, trauma to esophageal musoca through ingestion of dust and silica particles, consumption of hot beverages, and dietary constituents such as mycotoxins produced by fungi favored by environmental conditions and, possibly, extraneous carcinogenic seeds in wheat. (13 Refs)

145. THE NEGLIGIBLE ROLE OF ALCOHOL AND TOBACCO IN ESOPHAGEAL CANCER IN IRAN - "A CASE CONTROL STUDY" (MEETING ABSTRACT). (PP. 17-18)

Mahboubi E, Day NE, Ghadirian P, Salmasizadeh S
Eppley Inst. for Res. in Cancer, Omaha, NE 68105 U.S.A.
Third International Symposium On Detection And Prevention Of Cancer. 1976.

A study of 140 esophageal cancer patients and 288 healthy controls in Iran investigated the role of alcohol consumption and smoking and chewing of tobacco in esophageal cancer. The effects of these substances were analyzed with special emphasis on the age, sex and ethnic backgrounds of subjects surveyed. The findings were as follows: (1) Alcohol - Of 66 female patients interviewed, only one had consumed alcohol, while 17 of 67 males used alcohol (15 of these subjects were Persian and the others, Turkomans and/or Turkic-speaking people. The latter used alcohol moderately by comparison with 3 controls). There was clearly no association with esophageal cancer. (2) Tobacco - Three female patients and 27 male patients smoked, compared to 45 smokers among controls. Cigarette smoking was clearly not associated with the disease among Turkomans and Turks. However, among the Persian-speaking population, there were a number of heavy smokers, but this figure was not statistically significant. Another suspected causative agent was a substance called "nass" commonly used by central Asians at high risk for esophageal cancer. Analysis showed no association with the disease among Turkomans and Turks, but among Iranians, it was indicated that nass may have increased the risk. However, since less than 6% of the patients chewed nass, it apparently contributed little to the overall incidence. Methods of interviewing and control selection will be discussed. (Author Abstract)

146. OESOPHAGEAL CANCER STUDIES IN THE CASPIAN LITTORAL OF IRAN: RESULTS OF A CASE-CONTROL STUDY.

Cook-Mozaffari PJ, Azordegan F, Day NE, Ressicaud A, Sabai C, Aramesh B
Medical Res. Council External Staff, Dept. Regius Professor Medicine, Univ. Oxford, Oxford, England
Br J Cancer; 39(3):293-309 1979

A case-control study was conducted in northern Iran where very high rates of esophageal cancer (EP) occur among both men and women, to study factors identified in a previous study as potentially causally related to EP. Information was obtained by questionnaire and by interview. Other tumors (lung, stomach, breast, large bowel, larynx, and pharynx) were included to distinguish findings specific for EP from the general characteristics of cancer patients and to verify that expected associations, such as between lung cancer and cigarette smoking, would emerge under the prevailing field conditions. Each patient had two controls matched for village of residence, age, sex, and language group. Reinterviewing was performed to a limited extent to assess the accuracy of replies to questionnaires. The following were found not to be associated with EC: consumption of sheep's milk, yoghurt, wild spinach, and sesame oil; chewing of nass (tobacco and lime mixture), a habit confined to men; carpet-making; consumption of a special foodstuff (crushed pomegranate seeds, pepper, and raisins) during pregnancy; and salting and sun-drying of meat. The use of opium, bread, and tea could not be assessed in the retrospective framework. Strongly associated with EC risk were low socioeconomic status and a low intake of fresh fruits and vegetables. The two factors had an independent effect, and they were more marked for EC than for the other tumors. (13 Refs)

147. CANCER MORBIDITY AMONG TWO MALE COHORTS WITH INCREASED ALCOHOL CONSUMPTION IN FINLAND.

Hakulinen T, Lehtimaki L, Lehtonen M, Teppo L
Finnish Cancer Registry, Helsinki
J Natl Cancer Inst; 52(6):1711-1714 1974

The correlation between alcohol consumption and morbidity from cancer was investigated in two male Finnish populations. For the first population, the files of the Finnish Cancer Registry on cancer of the esophagus, liver, and colon (1965-1969) and lung (1968) in males were checked against the files of the "alcohol abuser" registry, a group totaling about 205,000 males. Excess morbidity was observed from cancer of the esophagus, liver, and lung but not from cancer of the colon. For the second population, the files on a group of chronic skid row alcoholics, numbering about 4370 annually in 1967-1970, were checked against those of the Finnish Cancer Registry (1967-1970). Excess morbidity was observed from cancer of the pharynx, esophagus, and lung; excess total cancer morbidity was also noted. The results agree with the hypothesis of a correlation between alcohol consumption and morbidity from cancer of the pharynx, esophagus, and liver. The high incidence of lung cancer in both populations may be attributed to concomitant heavy smoking, which may also be partly responsible for the excess morbidity from esophageal cancer.

148. ASSOCIATIONS OF BRONCHIAL CANCER AND CANCER OF THE UPPER AIRWAYS AND DIGESTIVE TRACT.

Level MC, Bureau G, Diem JL, Berlot P, Dubois de Montreynaud JM
Service de Pneumophtisiologie, C.H.U., 45, rue Cognacq-Jay, 51090 Reims Cedex, France
J Fr Otorhinolaryngol; 27(1):27-30 1978

In a 30-mo period from June, 1974 to December, 1976, oral endoscopically identified bronchial cancers in 210 patients were histologically confirmed in 155 patients. Cancers of the esophagus or upper respiratory tract (URL) were concurrent with (2) or preceded (10) the bronchial cancer in 12/210 patients (5.7%). The URL cancer preceded the bronchial cancer by 1-3 yr in eight patients, by 5 yr, in one patient, and by 15 yr in one patient. The 12 patients were men with an age range of 44-75 yr, and 8/12 had a history of heavy use of alcohol and tobacco. The histology of the cancers at the two sites was the same in all but three patients. Only 4/12 patients are still alive, and the period since diagnosis has been less than 1 yr for 3 of these patients. It has been proposed that concurrent or succesive cancers of the upper respiratory tract, esophagus, and bronchi are multicentric primary tumors affecting epidermal tissue of different organs.

149. ETIOLOGICAL ASPECTS OF CANCER OF THE GASTROINTESTINAL TRACT.

Lowenfels AB
New York Med. Coll., New York City, NY
Surg Gynecol Obstet; 137(2):291-299 1973

The likely causes of cancer of the gastrointestinal tract are reviewed. Certain carcinogenic agents have been found which are surprisingly site-specific. For example, polycyclic hydrocarbons, nitrosyl compounds and irradiation of the stomach lead to stomach cancer, and methylazoxymethanol induces cancer of the colon. Alcohol consumption and tobacco smoking are the chief factors related to cancer of the esophagus. Stomach cancer increases in frequency with distance from the equator and occurs in high rates in certain countries bordering the ocean. Furthermore, higher living standards and accompanying dietary factors were associated with lower mortality rates from cancer of the stomach. A negative association between stomach cancer and cancer of the colon has been found. Cancer of the large intestine is the most common gastrointestinal cancer and the survival rate is low, the 5 yr survival rate being less than 40%. High rates correspond to high levels of economic development. Migrant studies imply that environmental factors are more important than host factors. Dietary differences are the most likely explanation for variation in occurrence. It is likely that the agent responsible for cancer of the large intestine arises in the colon, and its activity is enhanced by prolonged contact of fecal material and the colon due to refined diet. Cancer of the small intestine is uniformly rare throughout the world, occurring with 2.5% the frequency of cancer of the stomach or cancer of the colon. Evidence indicates that an intestinal immune system offers protection and that an intestinal microsomal system might afford additional security against ingested foreign substances. Familial occurrence and association of certain genetic diseases with gastrointestinal carcinomas implicate genetic factors in carcinogenesis, although evidence indicates that environmental causes outweigh hereditary causes.

150. ESOPHAGEAL CARCINOMA IN BLACKS: ANALYSIS OF 88 NECROPSIED CASES.

Sampson CC, Braxton EL
Howard Univ. Hosp. and Coll. Medicine, Washington, DC
J Natl Med Assoc; 68(4):278-280,311 1976

The records and necropsy files of 88 patients (71 men, 17 women, ages 41-76 yr) dying from esophageal carcinoma during the 19-yr period from 1957 to 1975 were studied. All of the patients were black, coinciding with the observation that American blacks show a greater risk of developing esophageal carcinoma than other ethnic groups. All of the carcinomas were of the squamous type, and the histological variations ranged from well to poorly differentiated. Seventeen (19.3%) were located in the upper third, 41 (46.6%) in the middle third, and 30 (34.1%) in the distal third of the esophagus. Over 85% of the subjects had unskilled occupations, 53.4% were cigarette smokers, and 62.9% were alcohol drinkers. The increase in incidence in American blacks appears to be correlated with increased alcohol consumption and tobacco use. The incidence in American black men has risen from 7.5/100,000 in 1947 to 15.1/100,000 in 1969; in contrast, the rate in American white men has decreased from 6.1/100,000 to 4.4/100,000 over the same period. A similar but less dramatic change has been noted in black and white women. The etiology of esophageal carcinoma appears to be multifactoral, with no one entity accounting for all instances of the disease.

151. ETIOLOGICAL AND ENVIRONMENTAL FACTORS.

Wynder EL, Mabuchi K
No affiliation given
JAMA: 226(13):1546-1548 1973

The relationship of alcohol consumption and smoking to increased risk of esophageal cancer is discussed, and the demographic distribution of esophageal cancer is reviewed. High rates of esophageal cancer in France, particularly Brittany and Normandy, and in the Caribbean area have been linked to high alcohol consumption, in South African Bantus to the particular type of alcohol consumed, in India and Ceylon to nutritional deficiencies and betel chewing, and in northeastern Iran possibly to ethnic origins. Members of religious groups that forbid smoking and drinking have low incidences of this disease. Smoking is apparently directly carcinogenic due to the presence of numerous carcinogenic agents in tobacco smoke. Although alcohol is apparently not carcinogenic per se, its role in carcinogenesis may be related to the nutritional deficiencies often associated with alcoholism. Chronic deficiencies in vitamin B complex or iron are particularly implicated. The reduction, elimination, or modification of these risk factors would appear to prevent a number of cases of this disease. (no Refs)

152. ESOPHAGEAL CANCER AND ENVIRONMENTAL FACTORS (MEETING ABSTRACT). (P. 280)

Okada H, Aoki K, Shimizu H, Kuroishi T, Tominaga S
Dept. Preventive Medicine, Nagoya Univ., Sch. Medicine, Showa-ku, Nagoya 466, Japan
Proceedings of the 37th Annual Meeting of the Japanese Cancer Association held in Tokyo, Japan, August, 1978 Japanese Cancer Association, Tokyo, Japan, 283 pp., 1978.

There is more than a 100 fold difference in the rate of incidence of esophageal cancer between some particular areas of Japan, suggesting the participation of environmental factors for this disease. In order to elucidate the reason for the occurrence of esophageal cancer, case-control study has been conducted in Wakayama Prefecture, where the death rate is high and in Aichi Prefecture, where it is low. From the results of 200 cases (100 patients and 100 controls) obtained in each prefecture, the highly significant environmental factors (p less than 0.05) with a relative risk of over 2 were as follows: (1) Favors pork (7.4), (2) smokes (6.6), (3) eats bread for breakfast (4.3), and (4) favors noodles (3.2), in Aichi Prefecture and (1) uses soy sauce for seasoning pork or chicken (19.6), (2) takes hot tea gruel (10.0), (3) heavily salted foods (4.2), (4) smokes (3.7), and (5) drinks alcoholic beverages at supper (3.3) in Wakayama Prefecture. The factors with a relative risk of 0.5 and below were (1) cabbage (0.1), (2) medicinal wine (0.1), and (3) cola drinks (0.4) in Aichi Prefecture and (1) tomato (0.2), (2) fruit juice (0.3) and peanuts (0.3), (4) peaches (0.4), and (5) bean sprouts in Wakayama Prefecture. The factors related to the occurrence of this disease greatly differed in the two prefectures and the only common factor was smoking. As a whole, under-nutrition and low living standards are considered to be the risk factors. (no Refs)

153. OESOPHAGEAL CANCER IN INDIAN JEWS IN BEERSHEBA, ISRAEL (MEETING ABSTRACT).

Odes HS, Krawiec J
Gastrointestinal Unit, Soroka Medical Center, Beersheva, Israel
Digestion: 16(3):266 1977

A retrospective study revealed that 21 cases of esophageal carcinoma were seen at this hospital in the period 1961-1977. Jews of Indian origin accounted for 43% of the cases and the non-Indian group (North African, Near Eastern and European Jews) for 57%. Indian Jews constitute 4% of the population served by this hospital, so this group has a disproportionate incidence of esophageal carcinoma. The age of presentation (mean +- standard error of the mean) for Indians was 53.5 +- 2.5 years and for non-Indians 65.5 +- 2.9 years (p less than 0.01). The male:female ratio differed in the groups, and was for Indians 3:6 and for non-Indians 8:4. The histological diagnosis, available in 20 cases, was squamous cell carcinoma (8 Indians, 10 non-Indians) and anaplastic carcinoma (1 in each group). There were no cases of adenocarcinoma. The clinical features were similar in both groups and the prognosis was uniformly bad. Three etiological factors, malnutrition, alcoholism and excessive smoking, may account for the increased prevalence and earlier appearance of esophageal cancer in our Indian Jews.

154. NUTRITIONAL MODULATION OF CARCINOGENESIS. (PP. 665-691)

Newberne PM, Rogers AE, Gross RL
Dept. Nutrition Food Science, Massachusetts Inst. Technology, Cambridge, MA
Third International Symposium on the Detection and Prevention of Cancer held by the International Study Group for the Prevention and Detection of Cancer in New York, April 26-May 1, 1976. Part I, International Study Group for the Prevention and Detection of Cancer New York, NY, Vol. 1, 1193 pp., 1977.

Based on epidemiologic studies that clearly reveal a change in the incidence of some forms of cancer when populations move from one geographic location to another and change food habits, evidence has accumulated to indicate that nutrition is associated with resistance or susceptibility to cancer. The following positive correlations between cancer in five major target organs and environmental risk factors have been conclusively established: (1) esophagus: heavy consumption of cigarettes and alcohol; wheat bread and tea consumption; (2) stomach: low socioeconomic status; consumption of salted, smoked, or fermented foods; decreased consumption of raw vegetables; (3) colon: increased consumption of meats, saturated fats, and highly refined carbohydrates with low dietary fiber and decreased vitamin A; (4) liver: decreased dietary lipotropes and increased dietary fat; consumption of toxins such as alcohol and mycotoxins and modified microsomal oxidases; (5) breast: higher socioeconomic status, with increased consumption of animal fat; obesity, or, more likely, both increased weight and height; potential increases in estrogen synthesis. It is hoped that through continued study, nutrition may soon be used as a major modifier in efforts toward the prevention of cancer. (76 Refs)

155. AETIOLOGICAL FACTORS IN OESOPHAGEAL CANCER IN SINGAPORE CHINESE.

De Jong UW, Breslow N, Hong JG, Sridharan M, Shanmugaratnam K
Unit Epidemiol. Biostat., IARC, Lyons, France
Int J Cancer; 13(3):291-303 1974

Analysis of a hospital-based case-control study of esophageal cancer among Singapore Chinese (composed of various dialect groups including Cantonese, Hokkien, and Teochew) revealed the following statistically significant risk factors for both sexes: (1) belonging to either Hokkien or Teochew dialect groups; (2) consumption of beverages at very hot temperatures prior to illness; and (3) smoking Chinese cigarettes. Additional risk factors for males included birth in China and the consumption of Samsu (Chinese wine).

Consumption of bread, potatoes, and bananas were at significantly lower levels in male esophageal cancer patients than in controls. Esophageal cancer was less common in males who attended school for more than 8 yr. Analysis of the joint influence of selected variables confirmed the strong effects of dialect group and beverage temperature for both sexes. For females the smoking of Chinese cigarettes remained a risk factor; for males, the consumption of Samsu. Smoking western-type cigarettes and consuming strong liquors were not significantly related for either sex. These findings suggest that esophageal cancer is more likely to occur among traditional Chinese who maintain dietary patterns which include Samsu and the drinking of beverages at hot temperatures, but avoid the bland foodstuffs (bread, potatoes, and bananas) not native to their culture. The greater risk in Teochew and Hokkien may be due partly to consumption of a greater number of beverages at "burning hot" temperatures compared with Cantonese and other dialect groups. However, these differences are based on subjective impressions which should be verified by actual temperature measurements of drinks consumed.

156. "DIALECT GROUP" VARIATIONS IN CANCER INCIDENCE AMONG CHINESE IN SINGAPORE. (PP. 67-82)

Shanmugaratnam K, Wee A
Host Environment Interactions in the Etiology of Cancer in Man. Doll R, Vodopija I, ed. World Health Organization Internatl Agency for Res on Cancer Lyon France, 1973.

The incidence of cancers of selected sites among various Chinese dialect groups in Singapore was determined in a survey of cancer registration data for the period 1968-1970. The incidence of cancers of the esophagus and stomach was significantly higher among Hokkeins and Teochews than among Cantonese. Compared with the first two groups, the Cantonese had a significantly higher incidence of cancers of the nasopharynx (both sexes) and breast and lung (females). The higher proportion of unmarried persons and smokers among Cantonese women may be related to their higher risks for lung and breast cancer. However, no satisfactory explanation exists for the higher incidence of esophageal and stomach cancer among Hokkiens and Teochews. Because the distinctive characteristics of the dialect groups (e.g., occupation, areas of residence, education and and economic status, dietary habits) are changing rapidly, investigations to determine the etiological factors responsible for the differences in cancer rates should be started immediately. (26 refs)

157. NUTRITION, ALCOHOL,AND ESOPHAGEAL CANCER.

Tuyns AJ, Pequignot G, Jensen OM
Centre International de Recherche sur le Cancer, 150, cours Albert-Thomas, F69372 Lyon Cedex 2, France
Bull Cancer (Paris); 65(1):59-64 1978

A study in Brittany, France,compared diet and alcohol and tobacco consumption in a group of 200 men with esophageal cancer with those controls. No major deficiencies were found, either in quantity or quality, in the diet of the cancer group. A definite correlation was observed between alcohol consumption and the incidence of esophageal cancer. Smokers also had a higher incidence of this cancer. A dose-response relationship existed independently for alcohol and tobacco and the incidence of cancer; however, the use of both had a cumulative effect on incidence. Surveys of the role of dietary factors in esophageal cancer in other areas,such as Iran, are reviewed. (24 Refs)

158. THE CASPIAN SEA STUDY (MEETING ABSTRACT). (PP. 17)

Kmet J
LARC Research Center School of Public Health, and Institute of Public Health Research Tehran, Iran
Third International Symposium On Detection And Prevention Of Cancer. 1976.

Ecologically oriented esophageal cancer studies in the Caspian Littoral of Iran have been incited by the great climatical diversity of the area, stretching over 1000 kilometers and comprising over 4 million people, from the semidesert Turkoman regions in the East to the Caspian rain belt in the West. Changes in soil types, natural vegetation and agricultural practices parallel the changing features of the climate. Esophageal cancer follows suit and a thirtyfold difference in the incidence between East and West has been observed in women and a tenfold in men, with the age adjusted rates in Turkomans close to 200 per 100,000, among the highest ever recorded. Smoking and drinking incriminated as etiological factors elsewhere play no role in the traditional rural Moslem society in the region, and no other clues were obtainable to mount the usual case-control studies. A broad-based comparison of the environment and way of life was therefore conducted in 1972-73 in 38 villages throughout the region, but no other environmental factors such as intake of opium or other home medicine or large amounts of hot tea were incriminated. On the other hand, the role of nutritional deficiencies seems to be of greater importance in regions of highest incidence, the diet being marginal in animal protein and very low in Vitamin A, B2 and C. In poor Turkoman families there was little else but bread and weak tea in their diet all year around. The search for known carcinogens, particularly for nitrosamines in food, remained unsuccessful. Traditionally, etiological studies in cancer were based on the prevailing tendency to zoom a priori the research field on specific working hypotheses which can be reduced to controlled laboratory experiments. In extreme complicated human situations such limited approach produced only very limited results. Esophageal cancer is no exception to the general rule that peculiar incidence patterns of a disease in a given population are the result of previous disease experience, environmental exposure and immunogenetic predisposition, modified by the conditions of the specific ecological setting. In trying to disentangle this web of causation systematically, two representative traditional rural areas have been selected for longitudinal population laboratory studies, one in Turkoman semidesert and one in the rain belt. A multidisciplinary, multifactorial and multidisease research is in preparation, trying to investigate the interplay between external and internal environments of the population groups experiencing extreme . differences in esophageal cancer risk. (Author Abstract)

159. CANCER OF THE ESOPHAGUS IN SOUTHERN IRAN.

Sadeghi A, Behmard S, Shafiepoor H, Zeighmani E
Dept. Radiology, Nemazee Hosp., Shiraz, Iran
Cancer; 40(2):841-845 1977

An epidemiological study of esophageal cancer in southern Iran covers the 5-yr period 1969-1973 and is based on hospital records. The minimal yearly incidence of esophageal cancer was 5-10 times higher than the yearly incidence in Connecticut for the age group 15-44. In the age group 50-65+, the observed incidence rates dropped below those of Connecticut. Of the patients whose tumor site was recorded, 11/15 in the 20-34 age group and 13/52 in the 35-49 age group had a tumor in the upper third of the esophagus. The location of the tumor was related to age but not to sex, after taking age into account. The proportion of female esophageal cancer cases was significantly greater than that of the other gastrointestinal tract cancers combined. It appears that the risk in men and women in this region is nearly equal, but risk could conceivably be higher in women (similar to the appearance of the disease in northern Iran). The etiology of the disease in this region is not associated with tobacco smoking and/or alcohol use, since these habits do not correspond with the epidemiology of the disease. Iron-deficiency anemia and prolonged zinc deficiency may be possible etiological factors. (13 Refs)

160. CANCER OF OESOPHAGUS IN IRAN (MEETING ABSTRACT). (PP. 86-87)

Mojtabai A
Taj Pahlavi Cancer Institute, Tehran, Iran
Summary Program and Abstracts of Papers, Proceedings of the 3rd Asian Cancer Conference Held by the Philippine Cancer Society under the Auspices of the Asian Federation of Organizations for Cancer Research and Control in Manila, 26-30 September, 1977. Philippine Cancer Society, Manila, Philippines., 184 pp., 1977

Cancer of the esophagus is one of the commonest cancers seen in Iran. Geographical pathology and demographic aspects shows high incidence all over the country especially in the northeast and northwest of Iran. From an epidemiologic point of view the incidence of this disease is higher on the border of the Caspian Sea in Iran (2620/million), south of the Taihang mountains in northern China (1090/million), and in the Transkei, South Africa. Factors which play a role in the etiology of this disease are: environmental, nutritional, immunological factors, genetic markers, mutagenicity, opium, tobacco, parasites, etc. Prevention is the best way of dealing with this disease. Early detection and diagnosis of esophageal cancer in the earliest stage of disease before the patients become symptomatic is best. The results of such methods reduce mortality. (no Refs)

161. ESOPHAGEAL CANCER STUDIES IN THE CASPIAN LITTORAL OF IRAN: RESULTS OF POPULATION STUDIES - A PRODROME.

Day NE, Joint Iran-International Agency for Research on Cancer Study Group
World Health Organization, International Agency Res. Cancer, 150, Cours Albert-Thomas-69372, Lyon Cedex 2, France
J Natl Cancer Inst; 59(4):1127-1138 1977

Epidemiologic studies were undertaken to identify the geographic distribution of factors that might influence differences in esophageal cancer incidence along the Caspian Littoral of Iran. In zones of contrasting incidence and sex ratio, information was obtained on food intake, smoking and drinking patterns (including tea), and other personal habits; occupation, economic, and agricultural practices; and methods of food storage, preservation, and preparation. The diet in the highest incidence area was markedly restricted to bread and tea. The poor quality of the diet itself was thought to have a role in the increased risk of developing esophageal cancer. The use of opium and sesame oil, consumption of sheep's milk and yogurt, the chewing of nass (confined to men), and the use of dyes (confined to women) were also more prevalent in the high-incidence areas. Typical dietary items were analyzed for polycyclic aromatic hydrocarbons, volatile nitrosamines, aflatoxins, nitrates, and nitrites. No unusual levels or geographic differences were found for any of the carcinogens tested. (42 Refs)

162. CARCINOMA OESOPHAGUS IN NORTH KERALA.

Kumar KM, Ramachandran P
Med. Coll., Calicut, India
Indian J Cancer; 10(2):183-187 1973

Two hundred consecutive cases of carcinoma of the esophagus occurring in North Kerala, India were studied. Over half of the cases occurred between 41 and 60 yr of age, and the incidence in males was more than four times greater than in females. Nearly 65% of the cases presented a history of eating dried smoked fish; smoked fish; smoking and heavy tea drinking were also prevalent. The symptoms of esophageal carcinoma included dysphagia, regurgitation, retrosternal pain, and inanition. Radiological examination revealed three abnormal patterns: irregular narrowing, filling defect, and obstruction. Esophagoscopic examination revealed proliferative growth in 121 cases, irregular ulceration in 40 cases, narrowing with irregular mucosa in 25 cases, and nodules in 7 cases. Nearly half of the lesions were situated in the lower third of the esophagus. Histologically, the lesion was diagnosed as squamous cell carcinoma in 124 cases, adenocarcinoma in 36 cases, mucoid carcinoma in 7 cases, anaplastic carcinoma in 15 cases, and adenoacanthoma in 2 cases.

163. THE INTERPLAY OF FACTORS DETERMINING A CANCER PATTERN.

Rose EF
Bantu Cancer Registry, Transkei, South Africa
Prog Exp Tumor Res; 12:95-101 1969

In the Transkei, South Africa, over 4000 cases of esophageal cancer were reported to the Bantu Cancer Registry in 14 yr with a male:female ratio of 5:4. The staple diet of these people is maize, which is deficient in tryptophan and lysine; meat and milk are not part of the regular diet, and eggs are not allowed to most women. The possibility of lowered resistance to natural toxins due to this poor diet is discussed. The toxicity, tumorigenicity, and native uses of Senecio, cycads, berries of Solanum nigrum, tobacco and mycotoxins, as well as other physically irritating foods, is reviewed.

164. THE EFFECTS OF SOIL AND DIET ON DISEASE.

Rose EF
Bantu Cancer Reg., Butterworth, South Africa
Cancer Res; 28(11):2390-2392 1968

Possible reasons for the high but geographically varied incidence of esophageal cancer in the Transkei region are discussed: trace elements in the soil, dietary deficiencies (especially proteins), the uses of toxic plants as food and medicine (Senecio and cycads are mentioned), the widespread use of tobacco, and mycotoxins (throat swabs from cancer patients and persons without cancer yielded hyphae and pods, but attempts to culture throat fungi were usually unsuccessful). One possible relationship is that between esophageal cancer and the levels of available silica in the soil; in 89% of the high-incidence areas, the soil was of a high-silica type, whereas 64% of the disease-free areas were on low-silica soil. Persons in the high-silica soil areas would be exposed to large quantities of silica, both from corn meal (ground by stones) and from silica phytoliths.

165. OESOPHAGEAL CARCINOMA IN SRI-LANKA - IRON DEFICIENCY AS A POSSIBLE CAUSE OF ITS HIGH INCIDENCE AND ITS UNUSUALLY COMMON OCCURRENCE IN YOUNG FEMALES (MEETING ABSTRACT). (PP. 68-69)

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Summary Program and Abstracts of Papers, Proceedings of the 3rd Asian Cancer Conference Held by the Philippine Cancer Society under the Auspices of the Asian Federation of Organizations for Cancer Research and Control in Manila, 26-30 September, 1977. Philippine Cancer Society, Manila, Philippines, 184 pp., 1977.

A series of 372 cases of esophageal carcinoma, seen in the North and the Southwest of Sri Lanka are reviewed. Esophageal carcinoma is common in Sri Lanka, the standardized rates for the North of the country being 8.6 for males and 15.9 for females, as compared to 7.7 and 2.9, respectively for Japan. There was an unusual preponderance of women, the male: female ratio of 0.55:1 being the lowest in any reported series. The patients were relatively young, 43.8% less than 49 yr. This was more marked in the case of women. Pre-existing iron-deficiency was considered the most important etiological factor. External signs of sideropenic dysphagia were found in a large number of patients, particularly among females. Esophageal strictures, characteristic of sideropenia, co-existed with the carcinoma in 8.8% (11.9% in females). 6.3% had co-existing thyroid-nodules. These facts point to some abnormality in mineral absorption. Betel-chewing was found to be an important contributary factor in esophageal cancer, 78% of patients chewing betel, as compared with 29% of the general population had evidence of disease. The incidence of smoking was significantly higher in the male patients, as compared with the general population. A significant racial feature was also noted: a high incidence in Tamils of recent Indian origin. (no Refs)

166. ZINC LEVELS IN SERUM, HAIR AND TUMORS FROM PATIENTS WITH ESOPHAGEAL CANCER.

Lin HJ, Chan WC, Fong YY, Newberne PM
Dept. Pathology, Univ. Hong Kong, Hong Kong
Nutr Rep Int; 15(6):635-643 1977

The concentrations of zinc, copper, and iron in serum, hair and esophageal tissue of patients with esophageal cancer and healthy control individuals, was determined in Chinese men (45-75 yr old) by atomic absorption spectrophotometry. All the subjects had similar dietary histories and were in reasonably good health. Serum copper and zinc were determined by direct aspiration into the atomic absorption spectrophotometer and iron was determined as the ferrous-tripytidyl-s-triazine chelate in the atomic absorption spectrophotometer. Serum copper appeared to be slightly elevated in the cancer patients, whereas serum iron was lower (9.2 +- 3.3 micromole/liter as opposed to the normal value of 22.9 +- 6.7 micromole/liter). Reduced zinc levels were found in tumor tissue when compared with normal esophageal tissue, and the zinc concentration in the hair of the tumor patients was also lower than that of the normal subjects ($p=0.01$). These data and previously-proven esophageal lesions induced by zinc deficiency in experimental animals, suggest a relationship worthy of future investigation. (25 Refs)

167. NUTRITIONAL MODULATION OF CARCINOGENESIS. (PP. 665-691)

Newberne PM, Rogers AE, Gross RL
Dept. Nutrition Food Science, Massachusetts Inst. Technology, Cambridge, MA
Prevention and Detection of Cancer. Part I. Prevention. Vol. I. Etiology. Proceedings of the Third International Symposium on Dectection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 1193 pp., 1977.

Based on epidemiologic studies that clearly reveal a change in the incidence of some forms of cancer when populations move from one geographic location to another and change food habits, evidence has accumulated to indicate that nutrition is associated with resistance or susceptibility to cancer. The following positive correlations between cancer in five major target organs and environmental risk factors have been conclusively established: (1) esophagus: heavy consumption of cigarettes and alcohol; wheat bread and tea consumption; (2) stomach: low socioeconomic status; consumption of salted, smoked, or fermented foods; decreased consumption of raw vegetables; (3) colon: increased consumption of meats, saturated fats, and highly refined carbohydrates with low dietary fiber and decreased vitamin A; (4) liver: decreased dietary lipotropes and increased dietary fat; consumption of toxins such as alcohol and mycotoxins and modified microsomal oxidases; (5) breast: higher socioeconomic status, with increased consumption of animal fat; obesity, or, more likely, both increased weight and height; potential increases in estrogen synthesis. It is hoped that through continued study, nutrition may soon be used as a major modifier in efforts toward the prevention of cancer. (76 Refs)

B. Selected Clinical Observations Concerning Tobacco-Related Etiological Factors in Esophageal Cancer

168. EPITHELIAL DYSPLASIA IN CANCEROUS AND NONCANCEROUS ESOPHAGI.

Sato E, Tokunaga M, Sakae K, Mukada T, Sasano N
Second Dept. Pathology, Kagoshima Univ. Faculty Medicine, Kagoshima 890, Japan
Tohoku J Exp Med; 124(2):117-128 1978

The prevalence, severity, distribution, and histology of esophageal dysplasia were studied in 86 grossly normal human specimens obtained at necropsy and in 100 specimens of esophageal carcinoma obtained at surgery. Fifty-four of the necropsy specimens showed dysplasia, 32 from men and 22 from women. Seventeen men and three women showed moderate or severe dysplasia or carcinoma in situ (CIS). The incidence and severity of dysplasia seemed to increase with alcohol and cigarette use, but the results were inconclusive. The incidence and severity also increased with age. Chronic inflammation, glycogenic acanthosis, and hyperplasia of the duct epithelium were observed frequently, but they were not significantly related to the incidence of dysplasia. Most of the surgical specimens showed a more advanced dysplasia. Those that showed extensive dysplasia tended to have a mosaic pattern of CIS and dysplasia. Carcinoma + extensive dysplasia was found in 24 instances, carcinoma + multifocal dysplasia in 46. Of the 24 cases that did not have treatment prior to surgery, 15 showed dysplasia coexisting with the carcinoma, and 19 showed multicentric foci of carcinoma. The invasive carcinoma sometimes did not show a sharp demarcation from the surrounding mucosa, especially in cases involving well differentiated squamous cell carcinoma. The results indicate that dysplasia plays a significant role as a precursor lesion in esophageal carcinogenesis. (19 Refs)

169. ASSOCIATION OF SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK WITH CANCER OF THE ESOPHAGUS.

Goldstein HM, Zornoza J
Dept. Diagnostic Radiology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Am J Roentgenol; 131(5):791-794 1978

The association between esophageal cancer and squamous cell carcinoma of the head and neck region (oral cavity, pharynx, and larynx) was studied by reviewing hospital files for the period March 1944 to August 1976. Eighty-nine patients were found who had separate primary squamous cell tumors of the head and neck and of the esophagus, representing 10% of all patients with esophageal carcinoma evaluated at this institution. In greater than 80% of the patients, the separate primary tumors were discovered asynchronously (2 mo-16 yr apart). The expected number of esophageal carcinomas among the 10,000 patients with head and neck cancer was 10, compared with the 89 observed. The number of second primary tumors of the stomach and colon among the head and neck cancer population was not greater than anticipated. Most patients had a long-standing history of considerable cigarette and alcohol use. These findings suggest that alcohol and tobacco are etiologic factors linking these two primary cancer groups, and they indicate the importance of complete radiological evaluation of the esophagus in head and neck cancer patients. (8 Refs)

170. THE APPEARANCE OF SECONDARY ESOPHAGEAL CANCERS FOLLOWING TREATMENT OF PHARYNGO-LARYNGEAL CANCERS.

Gignoux B, Noel P, Haguenauer JP, Mayer M
Centre Leon Berard, 28, rue Laennec, 69373 Lyon Cedex 2, France
J Fr Otorhinolaryngol; 27(1):31-34 1978

A retrospective study of 5,903 patients with cancer of the upper respiratory tract (ORL) observed in the period 1960-1975 revealed 57 with cancer of the esophagus. Only cases in which the esophageal lesion was noted more than 6 mo after the ORL neoplasm were studied (6 esophageal lesions preceded the ORL lesion and 18 were simultaneous with the ORL lesion). The length of time before the appearance of the esophageal lesion was 6 mo-2 yr for 16 patients, 2-5 yr for 12 patients, and 7 to less than 10 yr for 5 patients. All men patients with a secondary esophageal lesion had a history of heavy use of tobacco and alcohol. Lesions of the upper one-third of the esophagus are considered to be extensions of the ORL lesion whereas lesions of the middle third or lower third of the esophagus are probably seeded from the mediastinal lymph node system. Treatment for the 33 patients included radiotherapy (18), chemotherapy (4), surgery (2) and combination radio- and chemotherapy (5). Av length of survival was 12-18 mo.

C. Chewing of Tobacco and Betel Nut as Related to Esophageal Cancer

171. ASSOCIATION OF VARIOUS CHEWING AND SMOKING HABITS WITH CARCINOMA OF THE OESOPHAGUS (MEETING ABSTRACT). (P. 105)

Jafarey NA, Zaidi SH
Jinnah Postgraduate Medical Center, Karachi, Pakistan
Third International Symposium on Oncology Held by Taj Pahlavi Cancer Institute in Tehran, 4-8 March, 1978. Taj Pahlavi Cancer Institute, Pahlavi Medical School, Tehran University, Tehran, Iran, 115 pp., 1978.

The type and frequency of use of various chewing (pan, tobacco) and smoking (cigarette, bidi, hookah) habits of 307 cases of carcinoma of the esophagus were compared with 3562 controls. The relative risk of chewing habits ranged between 3 to 8 times while those of smoking habits ranged between 3 to 29 times. Combination of habits carried a higher risk. (no Refs)

172. SOME OBSERVATIONS ON OESOPHAGEAL CARCINOMA IN CEYLON, INCLUDING ITS RELATIONSHIP TO BETEL CHEWING.

Stephen SJ, Uragoda CG
Gen. Hosp., Ratnapura, Ceylon
Br J Cancer; 24(1):11-15 1970

Epidemiologic data were studied for 237 patients with carcinoma of the esophagus, admitted to 2 hospitals in Ceylon (Ratnapurna and Kandy). Betel chewing was admitted by 90/111 patients questioned (81.1%). A survey of the population of 1 of the communities (Kandy) showed a much lower prevalence of betel chewing (328/1088 persons, or 30.1%). The patient group was preponderantly female (138/237 patients, or 58.6%). The av age at diagnosis was 46.9 yr in the women and 52.5 yr in the men; 23.2% of the women and only 10% of the men were under 40 yr of age at diagnosis. The middle third of the esophagus was the primary tumor site in 55.7%, the lower third in 33.3% and the upper third in 11.0%. At all 3 tumor sites, the incidence was higher in females than in males. The frequency of betel chewing in the population of Kandy was higher in females than in males (32.3% and 27.9%, resp). Since Ceylonese women seldom smoke tobacco or drink alcoholic beverages, the high frequency of esophageal cancer among Ceylonese women was attributed to betel chewing. It is noted that oral cancer, which has also been considered to be associated with betel chewing, is the most common malignant tumor in Ceylon (in the 12-mo period 1965-1966, the incidence rate for all of Ceylon was 28.3/100,000 population.

173. EPIDEMIOLOGY OF CANCER OF THE OESOPHAGUS IN INDIA.

Gangadharan P
Tata Mem. Hosp., Bombay, India
Indian J Surg; 36(8):293-298 1974

The incidence, mortality, distribution, and high risk factors associated with cancer of the esophagus in India were studied. Sources of data included the Bombay Cancer Registry reports for the greater Bombay area, the medical reports of the various Indian hospitals, and mortality rate figures. In the greater Bombay area, the incidence of esophageal cancer between 1964 and 1966 was 6.1/100,000 population for males and 5.1/100,000 population for females. In comparison with rates from other parts of the world these rates are quite high. The annual death rate from esophageal cancer in the Bombay area during this period was 4.2/100,000 population, esophageal cancer accounting for almost 10% of the deaths due to cancer. Cancer of the esophagus was especially frequent among Hindus from Maharashtra and Gujarat and among Moslems. The risk of esophageal cancer is significantly elevated among smokers and pan chewers, the risk being particularly among males indulging in both habits. These data indicate that esophageal cancer is an important problem in India and point to the need for further investigation into the epidemiology and risk factors associated with this disease.

III. GASTRIC CANCER

EDITOR'S NOTE: Section VII lists comparative epidemiological studies dealing with multiple cancer sites, including the stomach.

174. RELATIONSHIP BETWEEN TYPE OF TOBACCO USED AND LOCALIZATION OF TUMOUR IN PATIENTS WITH GASTRIC CANCER.

Zacho A, Nielsen J, Cederqvist C
Dept. Surgery, Finsen Inst., Copenhagen, Denmark
Acta Chir Scand; 141(7):676-679 1975

The relationship between the type of tobacco used and tumor localization was studied in 493 patients with gastric cancer. The relative frequency of the tumor site varied with the type of tobacco. In men who use all kinds of tobacco, a pipe was the most common form of smoking. Women smoked only cheroots or cigarettes or both. Men showed a significantly higher percentage of tumors of the cardia than did women. Women had a higher percentage of tumors involving the entire stomach. Men with tumors of the cardia were more often pipe and cigarette smokers than cheroot smokers while those with tumors of the entire stomach were more often cheroot smokers. Since the distribution among cheroot smokers was nearly the same in both sexes, the type of tobacco used might play an important role in the type of tumor; the same probably applies to pipe smoking, especially when combined with snuff or chewing tobacco, although these types were not used by women. Concurrent factors may also influence the localization of the tumor. (5 refs)

175. AN EPIDEMIOLOGICAL INVESTIGATION OF GASTRIC CANCER.

Wynder EL, Kmet J, Dungal N, Segi M
Sloan-Kettering Inst. Cancer Res., New York
Cancer; 16(11):1461-1496 1963

A study of gastric cancer was made based on concurrent interviews of male and female, resp, gastric cancer patients in: Japan (174 and 94); New York City (114 and 40); Iceland (48 and 9); Slovenia (31 and 20). In areas of high incidence of gastric cancer, common characteristics appear to be high intake of starchy foods (potatoes, rice and bread), with a concomitant low take of fresh fruits and vegetables. In some such areas there exists a relatively high use of home-smoked or charcoal-broiled foods. Results of the present study do not constitute evidence for or against a suspected relationship with vitamin A deficiency. Gastric cancer appears to occur more commonly in low socioeconomic groups; they tend to be more edentate (a finding most likely linked to nutritional deficiency). Among negative variables were tobacco and alcohol consumption, spices, rapidity of eating, mastication and temperature of food. Gastric ulcer plays a relatively minor, if any role, in the development of stomach cancer; however, achlorhydria, pernicious anemia and gastritis were not specially investigated in the present study. An extensive epidemiological review of clinical and experimental data is also presented.

176. EPIDEMIOLOGY OF STOMACH CANCER.

Hirayama T
Epidemiology Div., Natl. Cancer Center Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan
Gan Monogr Cancer Res; 11:3-19 1971

The results of an epidemiological study of stomach cancer in Japan are presented. These results are based on stomach cancer as a whole; future studies should present results by location in the stomach and by histological classification. In 1970, the mortality rate per 100,000 population was 58.4 for males and 36.5 for females, while the corresponding rates among US whites were 10.2 and 6.5. The trend of mortality rates with time was examined. The influence of age and sex, regional differences, age group, ethnic differences, socioeconomic status, occupation, and marital status on mortality rates is presented. The influence of various kinds of food and drink on stomach cancer incidence was analyzed, as was the influence of nutritional factors and regional variation, natural environmental factors including soil acidity, and of blood group type. Some general conclusions could be drawn from this study. It was found that the death rate and morbidity from stomach cancer was highest among the lower socioeconomic classes; this finding is thought due to nutritional deficiencies including vitamin A and calcium deficiency related to lower socioeconomic conditions. Consumption of locally favored foods high in salt content such as highly salted pickles (tsukemono) was positively associated with the stomach cancer death rate, while the reverse was true of milk and dairy-product consumption. A significantly higher mortality rate was found in males who both smoked cigarettes and drank green tea frequently. Other factors positively associated with stomach cancer death rate were smoking and a familial history of stomach cancer. (18 Refs)

177. ON THE EPIDEMIOLOGY OF GASTRIC CANCER.

Wolff G, Lauter J
Zentralinstitut fur Krebsforschung, Akademie der Wissenschaften der DDR - Robert-Rossle-Klinik, DDR - 1115 Berlin-Buch, Lindenberger Weg 80, East Germany
Arch Geschwulstforsch; 46(1):1-14 1976

A control group of 766 patients without conspicuous gastric disease and 257 surgical patients with histologically confirmed gastric carcinoma were interviewed with a standardized questionnaire for 32 variables. The two groups were compared by multivariate variance analysis. A univariate analysis of three other variables (blood groups, and tobacco habituation and type) is included. There were twice as many males as females in the cancer group and slightly more males among the controls; all patients were over 50 yr of age. The eight variables significantly linked with gastric cancer are listed in diminishing order: lower food intolerance (no food allergies), higher alcohol consumption, residential site (proximity to a metropolitan area), occupation (unskilled worker), early loss of teeth or longer use of dental prostheses, vehicular driving (private or occupational), absence of gallstones, and longer use of tobacco. Twelve other variables discriminated less significantly between control and cancer groups. Additional analyses matched 267 patients with normal gastric mucosa or negligible gastritis and 499 patients with chronic atrophic gastritis and the 257 cases of gastric carcinoma. The variable responses were nearly identical with those of the parent study. A special study comparing 81 females with confirmed stomach cancer and 367 random female controls followed the same pattern; in addition, a history of miscarriage was significantly linked to increased incidence of gastric carcinoma. The univariate assays showed a slightly higher incidence of blood group O and a slightly lower incidence of blood group A in stomach cancer, neither of which were significant. Smoking of cigars and/or cigarettes was significantly correlated with gastric cancer, and a higher lung cancer morbidity was found among all smokers. Direct contact between the gastric mucosa and exogenous carcinogens is implicated as the most important source of stomach cancer.

178. DIFFERENCES IN MALE AND FEMALE RATIOS ACCORDING TO THE SITE OF STOMACH CANCER AND ETIOLOGIC HYPOTHESES.

ANON
Ann Chir; 18(11-12):664-667 1964

In a survey conducted by the Interhospital Group of Paris from 1957-61, 298 out of 451 surgical cases of gastric cancer were selected in which it was possible to determine with accuracy the site of origin of the cancerous process. Of these, 194 occurred in men and 104 in women; the av age was 61 and 64 yr, resp. The male:female ratios according to site were: pylorus 1.5; body 2.7; fundus 3.6; and cardia 6.2; these differences were statistically significant. Analogous results were obtained in a similar analysis conducted among 1,311 cases of gastric cancer which were collected during 1943-60 in a previous study (Permanent Cancer Investigation). In this group the male:female ratios by site were: pylorus 1.8 greater curvature 1.9; surface 2.2; lesser curvature 2.4; cardia 5; and fundus 5. These differences in the sex ratios may be interpreted as the expression of etiological differences. It is suggested that tobacco and ethanol may play a role in the development of cancer of the fundus and cardia, as they do in cancer of the esophagus and upper respiratory tract.

179. GASTRIC CANCER.

Borges CC, Villalobos-Parez JJ
Nat. Inst. Nutrition, Mexico City
Rev Invest Clin; 20(1):11-23 1968

Pt records filed with the Mexican National Institute for Nutrition over a 20-yr period showed stomach cancer in 393/55,000 cases (349/393 confirmed histologically, the remainder by X-ray). The group of patients with cancer of the stomach accounted for (35.5%) of the total; other GI tumors involved the colon (21.7%), gallbladder and related structures (14.5%), pancreas (10.4%), esophagus (6.2%), liver 6/2%), duodenum and periampullar region (3.3%) and miscellaneous sites (2.2%). Of the patients with stomach cancer, 62% were male and 38% female (compared to 57% and 43%, resp, of the total patient population); the median age, at diagnosis was 56 yr and 30% were under 50. Possible etiologic factors were studied by comparing the stomach cancer patients with 500 healthy subjects. There was no apparent relationship between stomach cancer and the use of tobacco (46.5% of the patients and 46% of controls used no tobacco and about 20% of each group reported heavy use); 18% of the cancer patients and 3% of the controls were heavy drinkers, while 56% and about 67%, resp, did not drink. Deficient diets were reported by 30% of the cancer group and 8% of the controls. There was no demonstrable relationship between GI cancer and the ingestion of irritating foods or condiments such as chili. Approx. 9% of the stomach cancer patients had familial histories of cancer (g.i cancer in approx. 50%), compared to 6.5% and approx. 33%, resp, in controls. Personal histories of cancer were reported in 4 patients (1 man with skin cancer, 3 women with breast cancer) and none of the controls. Gastric acidity (studied in 250 cancer patients) was normal in 25%, high in 4% and low in 15%; antacidity was seen in 56%. X-ray studies showed evidence of prior peptic ulcer in 10.2% of the cancer patients (gastric ulcer in 8.2%), suggesting no significant correlation between the 2 disorders. Another study (previously reported) showed a higher incidence of blood type A in patients with stomach carcinoma than in patients with gastric ulcer.

180. CHANGING PATTERNS OF CANCER IN JAPAN WITH SPECIAL REFERENCE TO THE DECREASE IN STOMACH CANCER MORTALITY. (PP. 55-75)

Hirayama T
Epidemiology Div., Natl. Cancer Center Res. Inst., Tsukiji 5, Chuo-ku, Tokyo, Japan
Incidence of Cancer in Humans, Proceedings of the Cold Spring Harbor Conferences on Cell Proliferation. Vol. 4, Hiatt HH, Watson JD, Winsten JA, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Origins of Human Cancer., 602 pp., 1977.

The steady downward trend in age-specific death rates for stomach cancer in Japan is discussed. Almost no increase in mortality for cancer of all sites was observed in men during the last decade and a slight decrease was observed among women. The greatest decreases occurred in cervical cancer rates and in the rates of stomach cancer in both men and women. Sharp increases were observed for leukemia and for cancer of the lung, pancreas, prostate, urinary tract, colon-rectum, liver, breast, and ovary. The risk of stomach cancer was significantly increased in daily cigarette smokers and significantly reduced in those who ate green-yellow vegetables daily, and those who drank two glasses of milk daily. The decline in stomach cancer mortality appears to be due to dietary improvements and to the effect of early detection. The mortality rate for colon cancer and the colon cancer-rectal cancer ratio were highest in persons who consumed a small amount of rice daily and in daily beer drinkers. Increases in the breast cancer mortality rate may be due to a decline in the birth rate or to the rapidly increasing intake of dietary fat. Mortality from breast cancer was highly correlated with pork intake and, to a lesser extent, with animal fat intake. Daily cigarette smoking was the most important cause of lung cancer. Causes for changing patterns in the rates of other cancers are also discussed. (13 Refs)

181. THE INCIDENCE OF GASTRO-INTESTINAL CANCER IN NORTH BADEN (WEST GERMANY) 1971-1977.

Kayser K, Burkhardt HU
Dept. Documentation, Historic and Social Pathology, Univ. Heidelberg, Heidelberg, W. Germany
J Cancer Res Clin Oncol; 93(3):301-321 1979

The incidences of the cancer of the esophagus, stomach, small intestine, colon, and rectum during 1971-1977 in the district of North Baden, West Germany, are presented and their relation to environmental factors are discussed briefly. Esophageal cancer is rare in North Baden, and the male:female ratio is about 5:1. The causes are unknown, but there is some indication that high alcoholic consumption together with smoking leads to an increased risk. The risk decreases at greater than 70 yr of age. Gastric cancer comprises about one-third of all gastrointestinal (GI) cancers in this region. The male:female ratio has remained nearly constant over the study period, and it is about 1.6:1. Max risk occurs in the age groups 70-74 yr (men) and 75-79 yr (women). Approx 30% of these cancers are first diagnosed at surgery. Although great changes in food and living habits have occurred since 1910, the risk for developing gastric cancer has remained the same. Cancer of the small intestine is rare, with a total of 284 cases being found over the 7-yr period. Colon cancer comprises 25% of all the GI cancers, and there was a continuous increase in incidence from 1971 to 1977. More than one-half of all colon tumors are located in the sigmoid colon. Rectal cancer comprises approx 30% of all GI cancers, and max risk occurs at age 80-84 for men and 70-74 for women. The male:female sex ratio for this cancer increases more sharply with ascending age than that for colon cancer. The incidence is increasing much more slowly than that of colon cancers. The colon cancer incidence (per 100,000) increased from 18.2 in 1971 to 27.6 in 1977 in men an from 18.9 to 35. in women. The rectal cancer incidence 36.9 in men and 31.2 in women. The results of the pathoanatomic registry are agree well with the data from clinical registries. (41 Refs)

182. EPIDEMIOLOGY OF STOMACH CANCER IN DAGESTAN.

Dalgat DM, Aliev RG, Gireev GI, Abdulgamidov MM
Dagestan Med. Inst., USSR
Vopr Onkol; 20(2):76-81 1974

Stomach cancer was diagnosed in 964 patients, 517 males (52.5%, 19.1 per 100,000) and 447 females (47.5%), between 1966 and 1970. In Dagestan the male to female ratio was 1.1:1.0. The highest incidence of stomach cancer was in the 60-69 yr age group (88.1 per 100,000) and the lowest in those under 29 yr (0.2 per 100,000). Specific attention was paid to elucidating the environmental factors and eating habits in the areas with abnormally high incidence of the disease (3 mountainous regions with incidences of stomach cancer 32.0, 34.0 and 40.0 per 100,000 resp where 200 patients and 250 healthy adults were studied. Correlations between adverse eating habits and smoking and stomach cancer were confirmed. In particular, spiced food, pickles, fish, smoked products, overdone meat and excessive use of alcohol contributed to the disease. 74% of the patients had a history of precancerous diseases (peptic ulcers, gastritis, gastric polyposis). Soil and vegetation tests in areas with the highest incidence of stomach cancer showed excessive copper, cobalt, zinc, iron, boron, manganese and iodine.

183. A EPIDEMIOLOGICAL SURVEY OF CARCINOMA OF THE STOMACH IN MIE PREFECTURE. PARTICULARLY IN THE ISE DISTRICT).

Nomura S
Public Health Ctr., Ise, Japan
Mie Med Sci; 8(1):66 1964

In an extensive survey of death rates due to malignancies in 11 cities and towns in Mie Prefecture during a period of 11 yr ending in 1961, areas of high death rates were found such as Kise-machi and Kashiwazaki districts (standarized death rate of 123.9) and Tamaki-cho (rate 87.4) and also areas with low death rates (Ouchiyamamura, 48.2; Komato-cho, 67.5). On the basis of extensive studies of environmental and various endogenous and cultural factors, it was concluded that high death rates due to malignancies were correlated with high soil acidity and certain nutritional factors (increased intake of salt and carbohydrates; low intake of vitamins B1 and B2, animal proteins, fat, and calcium; high consumption of cereals, canned fish, "tsukudani" (seaweed), "miso" (soy bean product), soy sauce, dried fish and dark green vegetables; and low ingestion of poultry, milk, butter, "tofu" (bean cake), fried foods, and fruits). Smoking, alcohol intake and blood relatedness were not related to the high death rates.

184. THE EPIDEMIOLOGY OF GASTROINTESTINAL CANCER WITH SPECIAL REFERENCE TO CAUSATION.

Boyd J, Langman M, Doll R
Gut; 5(2):196-200 1964

The consensus of this demographic study is that the main causes of GI cancer arise from the diet; however, the evidence is only suggestive. Gastric cancer is common in Japan, Iceland, Finland, Poland, parts of the USSR, China and Chile; it is relatively rare in the USA (white population) and very rare among native populations in many parts of Africa, S. America and India. Where the stable food is maize, the disease is rare; where it is potatoes, it is common. Esophageal cancer is common in France, Switzerland, Finland, Iceland and the Karelian SSR plus extremely high incidences in localized areas such as the Transkei region of S. Africa, part of the Chinese province of Honan, Curacao and among the Bantu (within the last 30 yr). Three factors cited as important are tobacco, alcohol consumption and nutritional deficiency. Cancer of the large intestine is particularly common in Scotland and Denmark; rare in Israel and parts of Africa as well as in countries with a high incidence of gastric cancer. No particular factor was cited as a causative agent.

185. GASTRIC CARCINOMA. A CRITICAL REVIEW OF 243 CASES.

Olearchyk AS
5020 N. 11th St., Philadelphia, PA, 19141
Am J Gastroenterol; 70(1):25-45 1978

This review, of 243 patients with gastric carcinoma, includes 18.9% in TNM stage I, 8.2% in stage II, 26.3% in stage III and 46.5% in stage IV, 3.3% were early carcinomas. Age distribution was highest in the sixties (38.2%) and 85.2% were urban workers. Associated factors were alcoholism (26.7%), smoking (26.3%), benign gastroduodenal ulcers (14.4%), malignant tumors of the other organs (10.3%), family history of carcinoma (8.2%) and sideropenic anemia (45%). Predominant blood group was O (51.1%). There were 52.7% ulcerated, 36.6% polypoid or fungating and 10.7% diffuse or infiltrating adenocarcinomas. Predominant was antral (56.4%) pattern. Lesser curvature was a site of carcinoma 80.3%. Bone metastases were found in 7.8%. Reliable symptoms were weight loss (73.2%), epigastric, back or substernal pain (67.5%), hematemesis or melena (45.7%) and in carcinoma of the cardia or fundus, dysphagia or odynophagia (65.4%). Anemia was present in 51.6%, esophagogastroscopy in 68.6%, gastric cytology in 71.0% and combined in all. Complications were bleeding (21.9%) obstruction (17.2%), bleeding and obstruction (7.0%), perforation (2.9%) and gastric fistula (0.8%). Curative procedures were performed in 47.7% with 9.5% 5-yr survival which was 25.0% for stage I and 15.0% for stage II. Palliative procedures were done in 11.9%, diagnostic in 18.1% and none in 22.2% with no 2-yr survival. The 5-yr survival for proximal subtotal esophagogastrectomy was 10.0%, for total gastrectomy 7.7%, for distal subtotal gastrectomy 11.1% and for distal hemigastrectomy 6.2%. Overall 5-yr survival was 11 (4.5%) patients. There were 4.5% treated with adjuvant therapy with subjective and objective improvement in all. Primary cause of death in 72.0% was gastric carcinoma itself. Other primary cause of death was bronchopneumonia or lung abscess (5.4%), deep venous thrombosis and pulmonary embolism (4.6%), anastomotic or duodenal stump disruption (4.6%) and associated malignant tumors (4.6%). Misdiagnosis and delayed treatment occurred in 14.9%. Associated hiatus hernia was in 1.6%. The Thal-Nissen procedure was carried out on distal esophageal stricture due to extention of adenocarcinoma of the cardia thought to be benign in one (0.4%) patient. None of them survived 5 yr. (Author abstract) (70 Refs)

186. RESULTS OF TREATMENT OF 2000 CONSECUTIVE CASES OF GASTRIC CARCINOMA.

Bucalossi P, Veronesi U, Lomonaco F
Natl. Inst. for the Study and Treatment of Tumors, Milan, Italy
Acta Unio Int Cancrum; 19(6-7):1502-1505 1963

The present study evaluates the results of treatment of 2000 cases of gastric carcinoma at the Cancer Institute of Milan from June 1928 to December 1961. Of the cases reported, 1,365 were males and 635 were females; range of ages was 15-85 with highest frequencies between 55-59 yr for males and 60-64 yr for females. There was previous history of gastric ulcer in 101 patients and of duodenal ulcer in 21, indicating a positive correlation only between gastric ulcer and gastric cancer. A comparison of cigarette smoking in approx. 1,327 male gastric cancer patients and in 1000 male controls showed that 31.3 and 22.1%, resp, were heavy smokers (more than 20 cigarettes/day): 23.6 and 24.2%, resp, were moderate smokers (10-20 cigarettes/day): 27.5 and 30.4%, resp, were mild smokers (less than 10 cigarettes/day); 17.6 and 23.3%, resp, were nonsmokers. Among male patients, as compared to 1000 male controls, 54% vs. 48%, resp, consumed more than 1 liter/day of wine: 26.8% vs. 19%, resp, consumed more than 2 liters. Among women patients, consumption of wine did not differ from that of the general population. No conclusions were drawn with respect to either smoking or consumption of alcoholic beverages as possible contributory or etiologic factors in gastric cancer.

187. GASTRIC JUICE NITRITE: ITS SOURCE AND RELATIONSHIP TO HYDROGEN ION CONCENTRATION.

Walters CL, Hill MJ, Ruddell WS
British Food Manufacturing Industries Res. Assoc., Leatherhead, Surrey, England
IARC Sci Publ; (19):279-288 1978

Nitrite concentrations were determined in the fasting gastric juice (GJ) of 17 patients undergoing routine pentagastrin tests. Nitrite was present in the GJ from all 17 subjects, the mean concentration being 4.9 uM. Pentagastrin stimulation increased the volume and H+ concentration of the GJ and decreased the gastrin thiocyanate concentration from a mean of 0.9 to 0.3 uM after 30-45 min. However, there was no significant change from the basal level of the mean nitrite concentration of 4.9 uM throughout the stimulation period, in spite of increased gastric aspirate volumes. In GJ and saliva, the thiocyanate levels of smokers were significantly greater than those of nonsmokers, but, there were no significant differences in nitrite levels between the two groups. Patients with demonstrable gastroduodenal lesions could be divided into normals and hypochlorhydric (HCH) normals on the basis of their fasting H+ concentrations (greater than 15 and less than 5 mM, respectively). Neither mean H+ nor nitrite concentrations in the normals were significantly different from those of duodenal ulcer patients. H+ concentrations in the GJ of HCH normals were significantly lower and their nitrite concentrations were significantly higher than those of all groups other than the six gastric cancer patients. The mean GJ nitrite concentration of the gastric ulcer patients was significantly higher than that of normal and duodenal ulcer patients, and the H+ concentration was significantly lower. The six gastric cancer patients had a mean nitrite concentration significantly higher and an H+ concentration significantly lower than those of the gastric ulcer group. The difference in total bacterial counts and those of nitrate-reducing organisms among the diagnostic groups were secondary to those in H+ concentrations. (28 Refs)

188. GASTRIC CARCINOMA PROMOTED BY ALKALINE REFLUX GASTRITIS - WITH SPECIAL REFERENCE TO BILE AND OTHER SURFACTANTS AS PROMOTERS OF POSTOPERATIVE GASTRIC CANCER.

Domellof L
Univ. Hosp., S-901 85 Umea, Sweden
Med Hypotheses; 5(4):463-476 1979

For reasons that are not known, the incidence of stomach cancer is declining in most countries. In contrast, cancer of the gastric remnant after partial gastrectomy for peptic ulcer disease seems to be increasing. "Gastric stump cancer" has been claimed to be a separate disease entity and has recently been labeled an iatrogenic cancer. Postoperative mucosal degeneration, exposure to surfactants such as bile, deconjugation of bile salts by microflora, increased pH with the possible production of mutagenic compounds, and diet may contribute to the malignant transformation of target cells. The cancer risk seems to be higher in men. Differences in tobacco abuse and/or a sex-related metabolism of carcinogens (repair mechanisms) may explain this observation. Alkaline bile reflux is one important promoting factor, as judged by the occurrence of polyps and cancers in areas most exposed to the reflux. The decline in cancer incidence in the nonoperated stomach has mainly been restricted to intestinal-type cancer. Thus, it is important to note that stump cancer often is of the diffuse type. Different target cells and/or modes of carcinogen exposure may be of etiological importance in these histologically and clinically separate neoplastic diseases. (75 Refs)

189. ARE PATIENTS WHO ARE LESS SUSCEPTIBLE TO IMPAIRMENT OF PULMONARY FUNCTION BY SMOKING MORE PREDISPOSED TO DEVELOPMENT OF GASTRIC CANCER? (MEETING ABSTRACT).

Luk GD, Meyer MB
Dept. Medicine and Epidemiology, Johns Hopkins Univ. Sch. Medicine and Hygiene, Baltimore, MD
Clin Res; 26(4):613A 1978

The reciprocal relationship between the declining incidence of gastric cancer and the rising incidence of lung cancer suggests that they may be inversely related through some common factor. Inhaled particles are normally cleared from the lungs by mucociliary mechanisms and then swallowed. If these inhaled particles reaching the stomach via the lungs are potential carcinogens, gastric cancer patients might be expected to have better pulmonary functions, including mucociliary clearance, than lung cancer patients or normals. The pre-operative pulmonary function tests (PFT) of 12 gastric cancer patients with different smoking histories, were compared with the pre-operative PFT of 12 lung cancer patients and the PFT of 12 peptic ulcer patients and 12 normals. All the comparison groups were matched for race, age, sex, and smoking history. Results are tabulated. There is significantly less impairment of FEV1 by smoking in patients with gastric cancer than in those without. The degree of impairment of vital capacity by smoking is also significantly less in gastric cancer patients. These preliminary data suggest that further work in this area may be rewarding and may elucidate possible factors in the pathogenesis of gastric cancer. (no Refs)

IV. CANCER OF THE PANCREAS

EDITOR'S NOTE: Section VII lists comparative epidemiological studies dealing with multiple cancer sites, including the pancreas.

190. CANCERS OF THE PANCREAS AND BILIARY TRACT: EPIDEMIOLOGICAL CONSIDERATIONS.

Fraumeni JF
Natl. Cancer Inst., Bethesda, Md. 20014
Cancer Res; 35(11/Part2):3437-3446 1975

Epidemiological patterns for pancreatic and biliary cancers reveal more differences than similarities. Pancreatic carcinoma is common in western countries, although two Polynesian groups (New Zealand Maoris and native Hawaiians) have the highest rates internationally. In the United States, the disease is rising in frequency, predominating in men and in blacks. The rates are elevated in urban areas. The origin of pancreatic cancer is obscure, but a twofold increased risk has been documented for cigarette smokers and diabetic patients. Alcohol, occupational agents, and dietary fat have been suspected to be risk factors. The reported incidence of biliary tract cancer is highest in Latin American populations and American Indians. The tumor predominates in women around the world. In the United States, the rates are higher in whites than blacks, and clusters of high-risk counties have been found in the north central region, the southwest, and Appalachia. The distribution of biliary tumors parallels that of cholesterol gallstones (the major risk factor for biliary cancer). Insights into biliary carcinogenesis depend upon clarification of lithogenic influences, such as pregnancy, obesity, and hyperlipoproteinemia, exogenous estrogens, familial tendencies, and ethnic-geographic factors that may reflect dietary habits. Noncalculous risk factors for biliary cancer include ulcerative colitis, clonorchiasis, Gardner's syndrome, and probably certain industrial exposures. Within the biliary tract, tumors of the gallbladder and bile duct show epidemiological distinctions. Bile duct neoplasms predominate in men; they are less often associated with stones and more often with other risk factors. In some respects, bile duct and pancreatic tumors are alike. The male predominance of both tumors, an association between cholecystectomy and pancreatic cancer, and other considerations have prompted the notion that the same biliary carcinogens may affect the bile duct, ampulla of Vater, or (by reflux) the pancreatic duct.

191. I. SPECIAL SUBJECTS: I. CANCER OF THE PANCREAS, INTERNATIONAL MORTALITY TRENDS.

Aoki K, Ogawa H
Dept. Preventive Medicine, Nagoya Univ. Sch. Medicine, Nagoya, Japan
World Health Stat Rep; 31(1):2-27 1978

International mortality trends for pancreatic cancer in terms of age distributions, sex ratios, and other characteristics are reviewed based on information from the World Health Organization data bank. Geographic distribution, mortality trends, comparison of death rates by age and sex, and pancreatic cancer as a percentage of cancer at all sites are discussed. The countries of Northern and Western Europe, Northern America and Oceania have high rates, while countries of Southern Europe and the Balkan States have low mortality rates. Male preponderance in pancreatic cancer death rates in all countries and the narrow range of sex ratios between countries implies that some common etiological factors are working to predispose males to pancreatic cancer. In most countries, age-specific death rates increase linearly with advancing age from 30-40 yr old up to 75 old and over. The variation of sex ratio with age is relatively large before the age of 50, but smaller after menopausal ages. Risk factors thought to influence the development of pancreatic cancer include the amount of oils and fats consumed, the amount of meat consumed, alcoholic consumption, smoking, and occupational exposure to chemical substances. The data presented suggest that endogenous factors inherent to humans as well as environmental factors have significant effects on the development of pancreatic cancer. (52 Refs)

192. GEOGRAPHIC CORRELATES OF PANCREAS CANCER IN THE UNITED STATES.

Blot WJ, Fraumeni JF, Stone BJ
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20014
Cancer; 42(1):373-380 1978

Age-adjusted death rates for pancreas cancer during 1950-1969 were correlated by sex and race with demographic and industrial data for the 3,056 counties of the contiguous US. Only a small fraction of the county-to-county variation in mortality was explained by these variables, in contrast to their strong correlation with other common neoplasms. The only geographic cluster occurred in an area encompassing parts of Louisiana and Mississippi. Throughout the country, however, the rates for pancreas cancer were higher in urban areas, especially in men, and in counties with many residents of Scandinavian and East European (particularly Russian) descent. No associations were found with socioeconomic, industrial, or alcohol-consumption indices. The mortality patterns for pancreas and lung cancers were highly correlated in men, suggesting the influence of tobacco consumption on both tumors. In women, pancreas cancer was significantly correlated with diabetes mellitus, consistent with other evidence linking these two diseases. (23 Refs)

193. A COHORT ANALYSIS OF PANCREATIC CANCER, 1939-1969.

Benarde MA, Weiss W
Dept of Community Med and Environmental Health, Hahnemann Med Coll and Hosp, Philadelphia PA 19102.
Cancer; 39(3):1260-1263 1977

Pancreatic cancer mortality in the United States was examined by cohort analysis for the period 1939 to 1969. Birth cohorts at 5-year intervals were studied. White males and non-white of both sexes showed a shift of the cohort mortality rate curves by age toward younger groups as birth cohorts went from 1870-1874 to 1900-1904. This shift disappeared in white males and diminished in non-whites of both sexes between the cohorts of 1890-1894 and 1900-1904. The shift in non-whites was larger than in white males so that although non-whites had lower rates than whites in earlier birth cohorts, their rates exceeded those of whites in the most recent cohort. In the search for environmental cause(s) of pancreatic cancer, exposure characteristics should be compatible with these observations. (19 Refs). (Author Abstract)

194. AN EPIDEMIOLOGICAL EVALUATION OF THE CAUSES OF CANCER OF THE PANCREAS.

Wynder EL
Naylor Dana Inst. for Disease Prevention, American Health Foundation, New York, N.Y. 10019
Cancer Res; 35(8):2228-2233 1975

Recent epidemiologic evidence suggesting a relationship between diet and cigarette smoking to cancer of the pancreas is reviewed. Several prospective and retrospective studies have shown that the risk for pancreatic cancer is increased in cigarette smokers, but not in cigar or pipe smokers. Findings suggesting that dietary factors affect the development of pancreatic cancer include the increase of the cancer among Japanese immigrants to the U.S, the relatively high incidence among American Negroes and Jews, and a positive association between pancreatic cancer and high fat and/or cholesterol diets. Other factors of etiologic interest are the positive correlation between diabetes and cholecystectomy and pancreatic cancer in women, and the greater incidence of the disease (2/1 sex ratio) in men under 50. Two ways in which tobacco carcinogens could reach the pancreas are reflux from the bile duct into the pancreatic duct and distribution through the blood stream. Among the carcinogens that can be distributed by the blood stream are organ-specific nitrosamines, which produce pancreatic lesions in experimental animals. A third mechanism that would account for the increased risk of pancreatic cancer in smokers may be related to elevated serum cholesterol or lipid levels in smokers. The in vivo conversion of cholesterol to a cholesterol epoxide may be of etiological significance, although the carcinogenicity of such epoxides for epithelial tissue remains to be established. Two bile acids, lithocholic acid and taurodeoxycholic acid , were recently shown to act as tumor promotors in the colon of rats previously initiated with methylnitrosoguanidine . An attempt should be made in future epidemiological studies to identify reasons for the current sex ratio and the higher incidence of pancreatic cancer in blacks; studies should also be carried out to verify the data linking diabetes and gallbladder diseases to pancreatic cancer. It is recommended that tobacco manufacturers work toward a further reduction in tar and nicotine levels of cigarettes; food and agriculture industries are urged to work toward a reduction in the cholesterol content of eggs, and a reduction of the fat content of beef and milk.

195. EPIDEMIOLOGY OF CANCER OF THE PANCREAS.

Wynder EL, Mabuchi K, Maruchi N, Fortner JG
Amer. Hlth. Fdn., New York, N.Y.
J Natl Cancer Inst; 50(3):645-667 1973

Epidemiological features of pancreatic cancer were observed in a survey of 100 males and 42 females with adenocarcinoma of the pancreas, four males and seven females with islet cell cancer, and seven males and three females with cancer the ampulla of Vater. The sex ratio (male/female) for pancreatic cancer among patients of all ages was 2.4:1; the sex ratio for patients less than 50 yr old was 3.8:1. No significant differences were found between cancer and control groups in socioeconomic status. Cigarette smoking and cigar smoking were both associated with high pancreatic cancer risks. Among women, correlations with pancreatic cancer were found of early-onset diabetes and, possibly, for cholecystectomy. It was hypothesized that carcinogens in the bile act on the pancreas via reflux into the pancreatic duct.

196. PANCREAS CANCER (NON-ENDOCRINE): A REVIEW-PART I.

Cubilla AL, Fitzgerald PJ
No affiliation given
Clin Bull; 8(3):91-99 1978

Pancreas cancer is reviewed with emphasis on a retrospective study of 380 patients with duct cell carcinoma and a prospective study of 184 patients with possible cancer of the pancreas. Clinical features presented include age, sex, religion, use of cigarettes and alcohol, family history, and occupation. Diabetes, the most common recorded associated medical disease, was noted in 119/380 patients. Pathological findings presented are the site, stage, size, lymph node involvement, metastasis, gross appearance, histology, cytology, associated duct epithelial changes, and when a second primary tumor occurred in the patients. The mean survival period for patients with Stage I cancer was more than 2x that of patients with Stage II and 3x that of patients with Stage III. Median survival time was 1 mo in 102 patients who received no specific therapy other than laparotomy and biopsy of the primary tumor or of a metastatic lesion. The median survival period was 7 mo when a curative surgical operation was attempted. When chemotherapy and radiation therapy were the principal treatments, the median survival rates were 3 and 5 mo, respectively. (33 Refs)

197. PANCREAS CANCER (NON-ENDOCRINE): A REVIEW - PART II.

Cubilla AL, Fitzgerald PJ
Dept. Pathology, Sloan-Kettering Memorial Cancer
Center, New York, NY
Clin Bull; 8(4):143-155 1978

Findings from a retrospective and a prospective study of nonendocrine pancreatic cancer (PC) are reviewed. The increased risk of PC in diabetics is greater than that for any other cancer, especially in women. In the retrospective study, smoking significantly increased the risk in men. In neither study was there evidence that alcohol increased the risk, but tobacco and alcohol may be cocarcinogens in a small number of patients. There was no consistent combination of factors that might identify asymptomatic patients with early PC. Approx two-thirds of the patients in both studies had Stage III disease at diagnosis. The presence of marked atypia and carcinoma in situ in the duct epithelium adjacent to the cancers suggests that the duct cell is the origin of mucin-producing adenocarcinomas. The high incidence of perineural invasion probably contributes to the retroperitoneal spread and very poor prognosis. The incidence of carcinoma in situ in the duct epithelium of resected specimens suggests that there may be a sufficiently long in situ cancer phase, during which new techniques could be used to detect the disease. These techniques may include detection of pancreatic oncofetal antigen, determination of serum pancreatic ribonuclease levels, the leukocyte adherence inhibition assay, and ultrasonography. (85 Refs)

198. CANCER OF THE PANCREAS.

Howard JM, Jordan GL
Medical Coll. Ohio, Toledo, OH
Curr Probl Cancer; 2(3):3-52 1977

The incidence, pathology, clinical features, diagnosis, and management of pancreatic cancer are reviewed. For management purposes, it is suggested that pancreatic adenocarcinomas be classified according to whether or not they produce obstructive jaundice. In the US, pancreatic cancer ranks fourth among malignancies as a cause of death. Probable etiologic factors include smoking and exposure to industrial chemicals, such as nitrourethane, acetylaminofluorene, and methylcholanthrene. (51 Refs)

199. THE RISING INCIDENCE OF CARCINOMA OF THE PANCREAS: AN EPIDEMIOLOGIC APPRAISAL.

Krain LS
Los Angeles, Calif.
Am J Gastroenterol; 54(5):500-507 1970

Environmental and genetic factors in the incidence of cancer of the pancreas were investigated in an examination of mortality rate data for this condition. Age-specific death rates showed that death from cancer of the pancreas becomes markedly more frequent after the age of 45 yr and does not level off appreciably before the age of 85 or above; deaths/100,000 population from pancreatic cancer numbered 8 at the age of 45 yr and 32 at 60 yr. Female death rates from cancer of the pancreas approached male death rates 10 yr after menopause with female mortality increasing relative to male mortality after the age of 60. The numbers of male and female hospital admissions for pancreatic cancer are 9.6 and 6.4/100,000 population, resp, among Caucasians and 13.0 and 6.0/100,000 population for Negroes. Negro males have the highest incidence of cancer of the pancreas, and Japanese living in America have a higher incidence of the disease than do Japanese living in Japan. The latter finding confirms the importance of environmental factors in pancreatic cancer. The observed lack of relationship of the condition to menopausal or climacteric periods further minimizes a hormonal or genetic linkage for pancreatic cancer and suggests that exogenous factors are more important. Cigarette smokers who consume from 21-39 cigarettes/day were found to have a lower median age of occurrence of cancer of the pancreas than nonsmokers or light smokers. Death rates/100,000 population for smokers are 11 and 19, resp, for females and males aged from 45-65 yr; death rates for nonsmokers in the same age and category are, resp, 6 and 7/100,000 population. An inverse relationship was found between rank order of air pollution in 4 California cities and their incidences of pancreatic cancer; however, differences among cities were insignificant, and it was concluded that air pollution is not as closely related to pancreatic cancer incidence as is cigarette smoking.

200. THE RISING INCIDENCE OF CANCER OF THE PANCREAS - FURTHER EPIDEMIOLOGIC STUDIES.

Krain LS
Los Angeles, Calif.
J Chronic Dis; 23(10-11):685-690 1971

The incidence and distribution of cancer of the pancreas was investigated in a survey of cases recorded in the California Tumor Registry. The number of observed cases of pancreatic cancer recorded from public country hospitals was 784 among males compared to an expected number of 666 cases; on the other hand, the numbers of observed and expected cases of pancreatic cancer among male patients in private hospitals were 849 and 967, resp. A high incidence of pancreatic cancer was found among Negroes; the incidence in the Negro population in the study was 13 cases/100,000 population for males, while incidence for white and Chinese males were 9.6 and 11.1 cases/100,000, resp. The high Negro incidence did not explain the rising annual incidence of pancreatic cancer mortality in the United States, which has amounted to 300% since 1920. Some etiological factors which may be associated with the increased mortality are smoking, alcoholism and occupational exposure to carcinogens.

201. CANCER OF THE LUNG AND MOUTH IN SEVENTH-DAY ADVENTISTS. PRELIMINARY REPORT ON A POPULATION STUDY.

Lemon FR, Walden RT, Woods RW
Dept. Prev. Med., Loma Linda U. Sch. Med., Cal.
Cancer; 17(4):486-497 1964

In a study among California Seventh-Day Adventists (SDA) during 1955-1959, deaths from all causes and all cancers were 65% and 70%, resp, of the numbers expected, among the male SDA and 75% and 80%, resp, of the numbers expected, among the female SDA. Of the 3481 deaths (3451 with death certificates) reported over the period, 608 (224 men, 384 women) died from cancer and the frequency distribution by site for the men and women was as follows: miscellaneous, 29% and 29.6%, intestine and rectum, 14.7% and 16.7%; prostate and other genital areas, 13.4% and - ; breast, - and 17.7%; stomach, 11.2% and 5.7%; pancreas and liver, 10.3% and 10.7%; lymphatic and hematic, 9.4% and 9.1%; urinary tract, 5.8% and 2.9%; lung, 5.8% and 1.6%; bucca and pharynx, 0.4% and 0.5%; uterine cervix, - and 5.5%, resp. In unpublished California Public Health Department records on 52,071 men and 46,540 women who died from cancer, lung cancer ranked first (disregarding miscellaneous sites) as the cause of death (13.8%) in the men and breast cancer (20.5%) in the women, while cancers of the bucca and pharynx comprised 3.5% and 1.3% of the California men and women, resp. Pancreatic and liver cancer was more frequent in SDA than in non-SDA. All SDA male deaths from epidermoid or anaplastic lung cancer occurred among individuals who were recent adult converts (6 or 7 within 5 yr or death) and all of whom had also been regular cigarette smokers of long duration.

202. CANCER OF THE PANCREAS.

Kalberer JT
Natl. Cancer Inst., Bethesda, Md.
J Surg Oncol; 6(1):1-8 1974

Following a review on financial support for research related to cancer of the pancreas, a brief summary is made of the current state of knowledge of pancreatic cancer. It is the 4th most common cause of cancer deaths in the U.S, with approx. 19,200 persons dying from it annually, and occurs mainly between the ages of 30 and 70 yr, the incidence increasing with age. Epidemiological studies have shown heavy cigarette smoking, chronic alcoholism, and exposure to certain industrial carcinogens to be associated with increased incidence of pancreatic cancer. A proposed classification of exocrine pancreatic carcinomas is presented, followed by a discussion on diagnosis. Therapy varies according to the degree of involvement of the tumor. If a pancreatic tumor is localized and adjacent tissues contain only limited or no metastases, surgical removal is recommended. The surgical procedures used for possible cure are total pancreatectomy and pancreatiduodenectomy (Whipple procedure). Only about 8% of patient with pancreatic cancer are eligible for these radical procedures and postoperative mortality rates are high. Two protocols are presently under study. One involves the use of 5-fluorouracil (5-FU) and radiation therapy as an adjuvant in patient with potentially curable pancreatic cancer. The other involves a controlled evaluation of high-dose (6,000 rads) radiation therapy, high-dose radiation plus 5-FU, and medium-dose (4,000 rads) radiation therapy plus 5-FU in patient with localized but unresectable disease. (9 refs)

203. PANCREATIC CARCINOMA. A REVIEW OF ETIOLOGIC CONSIDERATIONS.

Mainz D
Med. Coll. Georgia, Augusta
Am J Dig Dis; 19(5):459-464 1974

Several epidemiologic observations concerning pancreatic carcinoma are well established. The disease is increasing in incidence and, despite improved diagnostic methods, the outcome is usually fatal. Several etiological observations may be drawn from current research. The potential of chemical carcinogens for influencing development of pancreatic carcinoma in animals has been amply demonstrated. The increased incidence of the disease among humans exposed to certain industrial chemicals including methylnitrosourethane, acetaminofluorene, paradimethylaminoazobenzene, methylcholanthrene, betanaphthylamine and benzidine has been noted. The incidence of pancreatic carcinoma is 2.5 times more frequent and occurs 10 yr earlier in smokers than in nonsmokers. Carbohydrate intolerance is present in about 50% of the patients with pancreatic carcinoma which is a common form of malignancy in diabetics. It is suggested that patients with diabetes mellitus and calcific pancreatitis may have an increased incidence of pancreatic carcinoma. There is as yet no evidence that bacterial, fungal, or viral agents cause pancreatic cancer in humans. Oncogenic viruses have caused pancreatic sarcomas in animals. A relation between alcoholism and pancreatic carcinoma has not been firmly established. There seems to be no connection between carcinoma of the pancreas and gallstone disease.

204. A CASE CONTROL STUDY OF CANCER OF THE PANCREAS.

Wynder EL, Mabuchi K, Maruchi N, Fortner JG
Div. Epidemiology, Naylor Dana Inst. Disease Prevention, American Health Foundation, New York, NY
Cancer; 31(3):641-647 1973

A retrospective epidemiological study was undertaken in 100 males and 42 females with adenocarcinoma of the pancreas and 307 sex-, age-, race-, and hospital-matched controls. The results showed that this cancer predominated among males, particularly at ages under 50, and was significantly associated with cigarette smoking. An association to cigar smoking was suggested. Among women, a significant association with early-onset diabetes was found, and there was a suggestive association with a history of cholecystectomy. The epidemiological data along with the pathological data suggested a working hypothesis that the bile may contain carcinogens which would be refluxed into the pancreatic duct exerting a carcinogenic effect. (Author abstract) (42 Refs)

205. ENVIRONMENTAL FACTORS AND DISEASES OF THE PANCREAS.

Longnecker DS
Dept. Pathology, Dartmouth Medical Sch., Hanover, NH, 03755
Environ Health Perspect; 20:105-112 1977

The role of environmental factors in the etiology of diseases of the pancreas is discussed. In the United States, the majority of cases of chronic pancreatitis result from chronic alcoholism. The possibility that cystic fibrosis is the result of a common mutation which is continually being introduced into germ cells in the general population is discussed. Developmental abnormalities including agenesis of the exocrine pancreas and selective trypsinogen deficiency have been described which could reflect teratogenic effects of external agents; however, no constant etiologic relationships have been established. Several epidemiologic studies suggest that chemical carcinogens may induce pancreatic cancer in humans. Increased incidence of pancreatic cancer has been shown among workers exposed to beta-naphthylamine or benzidene. There is also an increased incidence among chemists who belong to the American Chemical Society and among cigarette smokers. Chemical agents that are known or suspected to induce acinar cell damage or necrosis, to alter acinar cell or duct cell function, or to induce neoplastic change in the pancreas are listed. Therapeutic agents reported to have caused pancreatitis in humans are tabulated. Islet cells are subject to damage by viral infections and toxic chemicals. The incidence of diabetes increases with age and might be related to 'aging' of islet cells. Recommendations for detecting and reducing environmental factors that are involved in the etiology of diseases of the pancreas are presented. (72 Refs)

206. EPIDEMIOLOGY OF PANCREATIC CANCER.

Ishii K, Nakamura K, Ozaki H, Yamada N, Takeuchi T
Natl. CAncer Inst. Japan, Tokyo
Jpn J Clin Med; 26(8):1839-1842 1968

Dietary habits and preferences were examined in 475 patients with cancer of the pancreas. Smoking and alcohol consumption were associated with an elevated relative risk, as well as high consumption of meats and low consumption of vegetables. No definite conclusions could be drawn from this study, but further studies of a larger group of patients are recommended.

207. CHRONIC CALCIFYING PANCREATITIS AND PANCREATIC CARCINOMA IN JAPAN.

Ishii K, Nakamura K, Takeuchi T, Hirayama T
Hosp. Inst., Natl. Cancer Ctr., Tokyo, Japan
Digestion; 9(5):429-437 1973

Etiological and epidemiological studies were conducted in Japan using 150 patients with chronic calcifying pancreatitis and 1070 patients with carcinoma of the pancreas. The male-to-female ratio of calcifying pancreatitis was 3.5:1, while that of pancreatic carcinoma was 1.9:1. The frequency of both diseases was significantly lower among professional managing and service workers and significantly lower among agricultural workers. The cigarette smoking frequencies and daily intake of alcohol were significantly higher in both diseases than among a group of control subjects. Among the pancreatic carcinoma patients, the daily intake of meat, fish, milk, and soybean paste soup were also significantly higher, while the daily intake of rice, vegetables, and pickles was significantly lower than among the controls. The daily intake of alcohol was greater in calcifying pancreatitis than in pancreatic carcinoma. Alcohol abuse was the most important etiologic factor in calcifying pancreatitis, with alcohol abuse being closely correlated with pancreatic dysfunction in this group.

208. PROGRESS REPORT. CANCER OF THE PANCREAS.

Morgan RG, Wormsley KG
Dept. Physiology, Univ. W. Australia, Nedlands, W. Australia
Gut; 18(7):580-596 1977

Various etiological factors influencing the development of pancreatic cancer include cigarette smoking, diet, diabetes mellitus, pancreatitis, and various chemical carcinogens (result of animal studies). The incidence, diagnosis, and prognosis of this cancer are also reviewed. (140 Refs)

209. PANCREATIC CANCER.

Moyle R
No affiliation given
Br Med J; 1(6109):378 1978

The number of pancreatic cancer patients registered in England and Wales increased from 3,070 in 1962 to 4,414 in 1970. This increase has been associated with cigarette smoking (10-15 cigarettes/day), diabetes mellitus, and diet. The increased incidence could also reflect improved diagnostic facilities, more complete registration, and an increase in the number of people in the age range most at risk. (no Refs)

210. EPIDEMIOLOGY OF CANCER OF THE PANCREAS.

Audigier JC, Lambert R
Centre d'Epidemiologie du CNRS LP 005440, Faculte de Medecine, avenue Rockefeller, 69373 Lyon Cedex 2, France
Ann Gastroenterol Hepatol (Paris); 15(3):159-162 1979

The pancreatic cancer mortality rate in France is 6/100,000 men and 3/100,000 women, and it accounts for 3% of the overall cancer mortality. An increased incidence of pancreatic cancer was seen in cigarette smokers, diabetics, and workers exposed to beta-naphthylamine and benzidine. Methylnitrosourethan, methylnitrosourea, 2,2'-dihydroxy-N-propylnitrosamine, and 7,12-dimethylbenz(a)anthracene induced pancreatic cancer in experimental animals. (27 Refs)

211. SOME DATA ON 280 PATIENTS WITH CANCER OF THE PANCREAS. FREQUENCY, PREVIOUS AND CONCURRENT DISEASES, EXOGENOUS FACTORS.

Dorken H
1st Clin. Med., U. Hamburg, Germany
Gastroenterologia (Basel); 102(2):65-77 1964

In a study of exogenous factors in pancreatic cancer, data were obtained on the habits and occupations of 150/280 patients with pancreatic cancer. Among 100 males (M) only 2 were nonsmokers, the remaining were usually heavy smokers; 30% were cigar smokers, 23% mixed (cigarette + cigar) smokers, 3% tobacco chewers. Seven were cigar makers by occupation. Of 50 females (F) only 10 were smokers. Little or no alcohol consumption was found in 13/100 M; in 30/100 M, regular to excessive alcohol consumption was reported (10/30 were habitual drinkers; 8/30 were bartenders or employed in the alcohol industry). Many were in metal industries (35/100 M).

V. CANCER OF THE URINARY TRACT

EDITOR'S NOTE: Section VII lists comparative epidemiological studies dealing with multiple cancer sites, including the urinary tract.

A. Epidemiological Studies of Tobacco-Related Urinary Tract Cancer

212. POPULATION TRENDS IN CIGARETTE SMOKING AND BLADDER CANCER.

Hoover R, Cole P
Harvard U. Sch. Public Hlth., Boston, Mass.
Am J Epidemiol; 94(5):409-418 1971

An association between cigarette smoking and bladder cancer has frequently been demonstrated. The causal nature of the association has, however, remained in doubt. Because of this, trends in smoking habits and bladder cancer experience were examined for successive birth cohorts of men and women in the United States, Denmark and England and Wales. Increasing rates of the disease were observed in populations characterized by an increase in smoking among successive birth cohorts. The association is consistent in both sexes, different nationalities and in urban and rural groups. This makes it unlikely that the findings result from an association both of smoking and bladder cancer with a third variable.

213. THE RELATIONSHIP OF BLADDER CANCER TO SMOKING.

Lilienfeld AM
Dept. Chron. Dis., Johns Hopkins U. Sch. Hyg. Public Health, Baltimore, Md.
Am J Public Health; 54(11):1864-1875 1964

An extensive review of epidemiological and experimental studies of the relationship between smoking and cancer of the bladder is presented. It is concluded that an association is indicated by the evidence.

214. SMOKING AND BLADDER CANCER IN EGYPT.

Makhyoun NA
Dept. Urology, Francis Delafield Hosp., New York, N. Y.
Br J Cancer; 30(6):577-581 1974

A case control study was carried out on 365 Egyptian males to investigate the possible role of cigarette smoking in the etiology of bladder cancer. A smoking index measuring the intensity and duration of smoking was calculated. Patients were divided into two groups, 278 (76%) with previous chronic vesical schistosomiasis (bilharziasis) and 87 (24%) without past infection. The smoking index was significantly higher for both bilharzial and non-bilharzial patients with bladder cancer than for their corresponding non-cancer controls. In non-bilharzial patients a significant association was found between heavy and moderate smoking and bladder tumors; this confirms studies on patients in non-bilharzial countries. In bilharzial patients, however, the apparent association was not significant, due, possibly, to the younger age at which bilharzial subjects develop bladder cancer and to the lower income status of bilharzial subjects, who smoked fewer cigarettes. The local habit of water pipe smoking of "meassel" was not found to be significantly associated with bladder cancer. The results of the study support the view that cigarette smoking, particularly prolonged heavy smoking, is one of the factors in the etiology of bladder cancer.

215. PRIMARY EPITHELIAL TUMORS OF THE BLADDER IN THE FIRST TWO DECADES OF LIFE.

Javadpour N, Mostofi FK
Armed Forces Inst. Path., Washington, D. C.
J Urol; 101(5):706-710 1969

From 1945-1964 (inclusive), 10,000 primary epithelial tumors of the bladder were registered at the Armed Forces Institute of Pathology; including 40/10,000 from patients aged 6-20 yr. (36 males, 4 females; 1 Negro, 39 white); 3/40 were under 15. Histories of cigarette smoking (av. 1.5 packs/day), for 2-5 yr. (av. 3.7 yr) before the onset of symptoms, were noted for 18/40 patients, nearly all of whom were over 14. No histories of leukoplakia or exposure to other bladder carcinogens were recorded. Only 3 urinary tract infections were noted as the presenting symptom; 1 patient had schistosomiasis of the bladder. One patient had an adenocarcinoma and 1 patient (with schistosomiasis) had a squamous cell carcinoma. The other 38 tumors were of the transitional type, all in Jewett Stages 0 or A (TNM Stages X or T1); only 3/38 were infiltrative (the youngest of these 3 patients was 12 yr old, apparently the youngest recorded case of this type). Five tumors were papillomas; 35/40 tumors had papillary elements. The tumors in these young patients were histologically and clinically more benign than in older patients. A literature survey disclosed about 12 similar cases of bladder cancer in the first 2 decades.

216. EPIDEMIOLOGY OF BLADDER CANCER.

Yoshida O, Miyadawa M, Harada T, Okada K
U. Kyoto Sch. Med., Japan
Jpn J Clin Med; 26(8):1850-1854 1968

The relative risks of bladder cancer in smokers were studied in 192 patients with bladder cancer (163 men, 29 women) and in 222 control subjects (163 men, 59 women). Of the male patients, 92% were smokers and 8% were nonsmokers (compared to 77.3% and 22.7%, resp, in the male control group). Of the female patients, 37.9% were smokers and 62.1% were nonsmokers (compared to 13.6% and 86.4%, resp, in the female control group). The relative risks of bladder cancer in male and female smokers were calculated to be 3.4 and 3.9, resp. When the male cancer patients who smoked were compared to the male controls who smoked, the relative risk of bladder cancer in the heavy smokers was calculated to be 4.4. A graph of the steadily increasing age-adjusted bladder cancer mortality rates since 1955 is included; projection of this graph suggested that the bladder cancer mortality rates/100,000 population in Japan may be about 6.5 in males and 4.3 in females by 1985.

217. EPIDEMIOLOGY OF BLADDER CANCER (MEETING ABSTRACT). (PP. 44-45)

Pugh RC
Dept. Pathology, St. Peter's Hosp., London, England
National Cancer Week, Proceedings of the Australian Symposium on Nutrition and Cancer held in Adelaide, Australia, 20-24 November 1978. South Australian Postgraduate Medical Education Association Incorporated, 175 pp., 1978.

Though the main emphasis in this paper is on bladder cancer, it must be appreciated that a single type of epithelium lines the entire urinary tract and that a bladder tumor may follow, co-exist with, or antedate a tumor elsewhere in the tract. A serious difficulty in all epidemiological studies is the variation in the availability and reliability, and therefore comparability, of statistical data in different registries. The incidence of bladder tumor varies considerably from country to country and whereas it is relatively uncommon in the United Kingdom, it is the fourth commonest tumor in Iraq. Except in areas where bilharziasis is endemic bladder tumors are rare in the first five decades, but thereafter the incidence rises sharply with increasing age. In general, males are more often affected than females. In the United Kingdom the mortality rate rises with a decrease in social status. Urban/rural differences in incidence are recorded and in several countries there has been a steady rise in mortality within the last 60 yr. Environmental factors are thought to be more important than genetic ones in causing these altered trends. The aromatic amines have been incriminated in the dye-stuff, cable and other industries. There is good evidence that habitual smoking may cause bladder tumors and that renal pelvic carcinoma may be induced by excessive phenacetin intake. Tumors are also recorded as complications of the treatment of lymphomas with 2-naphthylamine-mustard and cyclophosphamide. Bladder tumor formation is a well recognized complication of certain local conditions in the urinary tract. The precise reasons why these tumors form are not yet known. It has been suggested that urinary nitrosamines may induce preneoplastic changes in the mucosa which, it is further postulated may progress to carcinoma under the added stimulus of other urinary carcinogens, mechanical irritation or repeated ulceration. (no Refs)

218. CIGARETTE SMOKING AND TUMORS OF THE URINARY BLADDER IN AUSTRIA (MEETING ABSTRACT). (PP. 311)

Kunze M, Kunze MJ
Austrian Fed Inst Pub Health and Inst Hyg, Univ Vienna, Vienna, Austria
Third International Symposium On Detection And Prevention Of Cancer. 1976.

Object of the study was the association of tobacco consumption and tumors of the urinary bladder. It was intended to contribute to the work by other groups by investigating a large number of cases (500) and by using a new model for the procedure of epidemiological control. The respective situation in Austria was studied thoroughly for the first time. In a retrospective type of study patients suffering from tumors of the urinary bladder were interviewed by a mail survey. Information gathered: smoking status (smoker, ex-smoker, never smoker) age when started to smoke; years of not smoking (ex-smoker); years of smoking (smoker and ex-smoker); life time consumption of cigarettes (smoker and ex-smoker); education; inhalation; occupational exposure. The data were compared with the respective figures for the Austrian population based on nationwide surveys performed by the Austrian Bureau of Statistics and the Austrian Tobacco Monopoly. A significantly higher portion of cigarette smokers was found among patients with bladder tumors than in the Austrian population. This result is the same for men and women as well as for patients suffering from carcinoma and papilloma. Additional findings were: smoking patients had started smoking earlier in their lives than average Austrian smoker. Patients who had given up smoking had done so later than the average Austrian ex-smoker. Patients with carcinoma and patients with papilloma showed no difference in respect to the duration and quantity of cigarette consumption. The inhalation habits were also found to be similar. The theoretical possibility of occupational exposure was found among 5% of all patients. The relative risk for men was 1.57 and 2.47 for women; for men over 60 years 1.75. (Author Abstract)

219. TAR EXPOSURE IN TOBACCO-ASSOCIATED LUNG AND BLADDER CANCER.

Kunze M, Vutuc C
Hygiene-Institut, Arbeitsgruppe Socialmedizin der Universitat, Kinderspitalgasse 15, A-1095 Vienna, Austria
Munch Med Wochenschr; 121(32/33):1041-1042 1979

A questionnaire study of smoking history was carried out in 200 men with lung cancer (group I) and 150 men with bladder cancer (group II). The av ages of men in groups I and II were 63.2 yr and 68.7 yr, respectively. Ninety-five percent of those in group I smoked cigarettes vs 87% of those in group II (p less than 0.01). Cigarettes of high tar content (greater than 25 mg) were currently smoked more frequently by group II patients than by group I (p less than 0.01) patients. Group II patients had smoked an av of 2.5 yr longer than group I patients. These observations suggest that the critical amount of exposure to smoking producing bladder cancer is higher than that leading to lung cancer. The use of high tar cigarettes was more prevalent in both groups, compared with the general population. The av tar content of cigarettes produced in Austria was 33.7 mg in 1960, and declining to 18.3 mg in 1975. Since 1965, the av content has been less than 25 mg. Evidence for possible exposure to carcinogens at work was found in only 6% of the patients, indicating that smoking is a more important cause of bladder and lung cancer in Austria than is occupational carcinogen exposure. (8 Refs)

220. SMOKING HABITS OF BLADDER CANCER PATIENTS: AN ATTEMPT TO QUANTIFY TAR EXPOSITION.

Vutuc C, Kunze M
Hygiene-Institut, Universitat Wien, Kinderspitalgasse 15, A-1095 Vienna, Austria
Aktuel Urol; 10(3):159-162 1979

The smoking habits of 150 men with cancer of the urinary bladder were studied. One hundred and thirty patients (av age 68.7 yr) were cigarette smokers (the av length of smoking was 42.7 yr), 1 was a pipe smoker, and 19 were nonsmokers. In the general population, the percentage of smokers and former smokers among men aged greater than 50 yr is 74.5%, ie, significantly lower. Among the cancer patients, 98% of the smokers smoked nonfilter cigarettes with a high tar content (greater than 25 mg) most of the time or exclusively (47%). In 52% of the cases, the last brand smoked was in this category. Of all brands smoked, the high-tar brands were smoked longest (av 37.4 yr). None of the smokers tended to prefer brands with the lowest tar content (less than 15 mg). Although sales of high-tar cigarette brands have decreased in Austria during the last several years, this trend was not applicable to the bladder cancer patients. The findings indicate that the risk of bladder cancer can be reduced substantially by reducing the tar exposure of the smokers, ie, by banning high-tar cigarette brands. (11 Refs)

221. PARALLEL MORBIDITY AGE-CURVES FOR NEOPLASMS OF THE LUNG AND BLADDER.

Clemmesen J, Bremerskov V
Danish Cancer Registry, Finsen Inst., Copenhagen
Biomedicine; 19(5):198-199 1973

Morbidity age curves for neoplasms of the lung and bladder among males living in metropolitan Copenhagen were constructed using data from the Danish Cancer Registry for the years 1943 through 1967. The age curves for the two neoplasms were nearly parallel, with a correlation coefficient of .97. The age curve for bladder tumors was, however, placed later in life than that for lung cancer, indicating a latent period of 9 to 10 yr longer with the former. In that previous data have shown that tobacco smoking is associated with bladder tumors among Copenhagen males, there is reason to assume a simultaneous oncogenic influence on both lung and urinary bladder.

222. CIGARETTE SMOKING AND CANCERS OF THE URINARY TRACT: GEOGRAPHIC VARIATION IN THE UNITED STATES.

Fraumeni JF
Epidemiology Branch, NCI, Bethesda, MD, 20014
J Natl Cancer Inst; 41:1205-1211 1968

Variation in bladder cancer mortality among states was highly correlated with the per capita cigarette sales estimated from state tax revenues. This relationship was independent of urbanization and similar in magnitude to that observed between cigarette consumption and cancer of the respiratory tract. In contrast, leukemia showed no correlation with cigarette consumption, whereas kidney cancer had an intermediate but significant relationship. These findings are consistent with other evidence relating the distribution of bladder cancer to smoking patterns of the population, and suggest that cancers of the upper urinary tract may also be associated with cigarette smoking. (Author abstract) (12 Refs)

223. SMOKING AND CANCER OF THE LOWER URINARY TRACT.

Cole P, Monson RR, Haning H, Friedell GH
Harvard Sch. Publ. Hlth., Boston, Mass.
N Engl J Med; 284(3):129-134 1971

The association of cigarette smoking and transitional or squamous cell carcinoma of the lower urinary tract was investigated in a survey of 470 cancer patients. More than 90% of the patients had bladder tumors. The age-specific incidence data for bladder cancer for males and females indicated that the risk of bladder cancer for men increases at a constant rate throughout life, while the risk for women began to increase after age 60. Male cigarette smokers had a relative risk of bladder cancer of 1.89 compared with nonsmokers and female smokers had a relative risk of 2.00. About 39% of male cases of bladder cancer were related to smoking, and about 29% of female cases were smoking-related. The highest number of bladder cancer cases among smokers occurred in male patients who smoked from 1/2-1 1/2 packs of cigarettes/day (140 observed cases). In both sexes, the risk of contracting bladder cancer was increased among smokers who inhaled deeply. Attributable risks of bladder cancer for smokers increased with age; risks for patients aged 20-59 yr, 60-74 yr, and 75-89 yr being, resp, 10, 60, and 87 cases/100,000 population. None of the excess risk of bladder cancer associated with cigarette smoking was explained by any indirect association with occupational exposure. It appeared likely that incidence rates for bladder cancer among women will increase in the next 10 yr. Pipe and cigar smoking was not associated with a significant risk of bladder cancer.

224. ANALGESIC ABUSE, RENAL PARENCHYMAL DISEASE AND CARCINOMA OF THE KIDNEY OR URETER.

Mahony JF, Storey BG, Ibanez RC, Stewart JH
Dept. Medical Res., Urology and Morbid Anatomy, Sydney Hosp., Sydney, Australia
Aust NZ J Med; 7(5):463-469 1977

In a consecutive series of 88 cases of carcinoma of the kidney and upper urinary tract seen at one hospital, 31 had malignant urothelial tumors of the renal pelvis or ureter. Forty-two per cent of these transitional-cell carcinomas occurred in patients with renal papillary necrosis following upon prolonged and heavy analgesic ingestion. Other possible etiological factors were heavy cigarette smoking (61% of cases), long-standing urinary obstruction or infection (23%) and possible occupational exposure (6%); in only four cases (13%) was there no identifiable etiological factor. Those cases with analgesic nephropathy were characterized by renal functional impairment, hypertension and interstitial nephritis, but there was no difference in the clinical behavior or pathological appearances of the tumors in the two groups. The clinical and experimental evidence that certain metabolites of phenacetin are carcinogenic is reviewed. (Author abstract) (45 Refs)

225. EPIDEMIOLOGICAL STUDY OF 314 CASES OF CANCER OF THE BLADDER IN THE ADMINISTRATIVE DEPARTMENT OF BAS-RHIN, FRANCE.

Bollack C, Poyot G
Service de Chirurgie Urologique, C.H.U., Strasbourg, France
Urol Res; 7(2):127-130 1979

The geographical distribution of 314 cases of bladder cancer among eight districts of the Department of Bas-Rhin in France was studied. Considerable variations in morbidity were observed, with an urban predominance possibly due to environmental factors. The average morbidity in two districts was 7.3 cases/100,000 residents, which was similar to the average for the Department as a whole. In two other districts, the average morbidities were 10 and 8.5 cases/100,000 residents, respectively, and in four districts the average was between 5.9 and 6.1 cases/100,000 residents. Among 180 patients studied more extensively, nine (5%) had second tumors diagnosed before, at the same time as, or shortly after the diagnosis of bladder cancer. Of five such patients with second tumors of the lung, pharynx, or mouth, five were heavy smokers. (11 Refs)

226. CORRELATION OF SITES. (PP. 87-100)

Clemmesen J
Danish Cancer Registry, Finsen Inst., Copenhagen 2100, Denmark
Incidence of Cancer in Humans, Proceedings of the Cold Spring Harbor Conferences on Cell Proliferation. Vol. 4, Hiatt HH, Watson JD, Winsten JA, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Origins of Human Cancer., 602 pp., 1977.

Patterns in the occurrence of malignant neoplasms in Denmark during the period 1943 through 1972 (data obtained from the Danish Cancer Registry) were analyzed. Although there was a considerable regularity in the patterns over the years, there were some outstanding changes: morbidity rates for cancers of the male digestive organs, particularly the stomach, have decreased, as has that for esophageal cancer; cancers of the pancreas, respiratory tract and lung, genitals (especially in men), breast (women only), urinary tract, skin, and hemopoietic system have increased. A socioeconomic grading for lung cancer among men and for cervical uterine cancer is unfavorable to the poor. Age-adjusted mortality rates showed a definite correlation between cigarette consumption and lung cancer and a less pronounced correlation between cigarette consumption and bladder cancer. The ratio of lung to bladder cancer in Denmark, Sweden, Norway, and the US was approx 3:1, whereas the ratios for Britain and Finland were considerably higher. There was no negative correlation between the morbidity rates for cervical and breast cancers in several countries, but reverse ratios appeared in Israel and Japan. (14 Refs)

227. TOBACCO AND CANCER.

Cousin M
Comite National Contre le Tabagisme, Paris, France
Lutte Cancer; (210):1-3 1976

The incidence of lung cancer has increased from 2/100,000 in 1930 to 50/100,000. Tobacco, particularly in the form of cigarette smoke, is implicated in carcinogenesis; 90%-95% of lung cancer patients are cigarette smokers. The risk of cancer increases with the number of cigarettes smoked, and cancer generally develops at about 125,000-150,000 cigarettes. Other environmental and occupational factors can predispose to lung cancer. Treatment is difficult, and survival is only 5%-10% after 5 yr. Tobacco is also implicated in cancer of the digestive system, the larynx, and the urinary system. (no refs)

228. CANCER BY COUNTY: NEW RESOURCE FOR ETIOLOGIC CLUES.

Hoover R, Mason TJ, McKay FW, Fraumeni JF
Epidemiology Branch, Natl. Cancer Inst., Bethesda, Md. 20014
Science; 189(4207):1005-1007 1975

To provide leads to the causes of cancers, cancer-mortality rates were collected for the 3056 counties of the contiguous U. S. The age-standardized mortality rates for 35 cancer sites were calculated from the age-, race-, and sex-specific rates for 1950-1969. The distribution of bladder cancer in white men so obtained is clustered in areas with heavy industry; this pattern was not duplicated in females. To characterize the possible hazards, 64 areas were selected in which: bladder-cancer mortality for men was significantly higher than the national rate, the male-to-female ratio of bladder cancer mortality was higher than the national ratio, and the lung-cancer rate among men did not differ significantly from the national rate. These criteria selected areas where bladder cancer is more likely to be related to industrial exposure than to cigarette smoking. The patterns obtained indicate that automobile and nonelectrical-machinery manufacturing are correlated with high incidences of bladder cancer. The known association with chemical industry was confirmed. Mapping of stomach-cancer mortality rates showed high rates in major cities and areas characterized by low socio-economic class, but also in rural counties with notable populations of Russian, Austrian, Scandinavian, and German descent.

229. AIR POLLUTION. (PP. 225-239)

Pike MC, Gordon RJ, Henderson BE, Menck HR, Soo-Hoo J
Persons at High Risk of Cancer, an Approach to Cancer Etiology and Control. Fraumeni Jr. JF, ed. New York, Academic Press, Inc, 554 pp., 1975.

The role of air pollution in carcinogenesis, particularly lung cancer, is reviewed. Measurements of benzo(a)pyrene (BP) concentrations in the atmosphere provide the most widely available indicator of polycyclic aromatic hydrocarbons, the main class of chemically identified carcinogens in the air. Two interferences in evaluating the possible effect of air pollution on lung cancer are cigarette smoke and occupational exposure to lung carcinogens. The results of a study of carbonization workers in a British gasworks indicate that each nanogram per cubic meter of BP causes $0.4/10^5$ extra lung cancer cases per year, so that a city with 50 ng/m^3 might expect to have an extra $18/10^5$ lung cancer cases per year. This estimate of a small general air pollution effect on lung cancer agrees with most other epidemiological evidence. Another study compared the lung cancer rates in Liverpool to those in rural North Wales and found that the urban effect produced an excess of $28/10^5$ lung cancer deaths in nonsmokers and $100/10^5$ such deaths in smokers. The difference in BP levels in the two areas was 70 ng/m^3, leading to the estimate that the air pollution effect in the presence of cigarette smoking was $1.4/10^5$ per ng/m^3 BP or $0.4/10^5$ per ng/m^3 BP in nonsmokers. These two studies support the notion of a proportional relationship between BP concentration in the air and lung cancer rate. Bladder and scrotal cancer are also linked to high levels of air pollution. Calculations are included that show that the excess lung cancer rate per ng/m^3 BP in air could be as much as 3.5 times greater in smokers than in nonsmokers; the differential effect apparently is not related to the absolute level of smoking. The intense, short exposure to polycyclic aromatic hydrocarbons through smoking a cigarette may maximally induce the aryl hydrocarbon hydroxylase (AHH) system in the lung. The low-level carcinogens in the air are then optimally transformed to their active form and do their greatest damage. The nonsmoker has a lower level of AHH activity in the lung, and thus air pollution carcinogens might be cleared via a less carcinogenic route.

B. Selected Clinical Observations Concerning Etiological Factors in Tobacco-Related Urinary Tract Cancer

230. CIGARETTE SMOKING AND CANCER OF BLADDER AND LUNG.

Dische S, Saunders MI, Lee M, Bennett MH
Regional Radiotherapy Centre, Mount Vernon Hosp., Northwood, Middlesex HA6 2RN, England
Br Med J; 2(6045):1174-1175 1976

Eight patients (all men, aged 59 to 76 yr) who developed more than one primary tumor resulting from cigarette smoking are presented. Each of the patients is classified as a heavy cigarette smoker. The original diagnosis was transitional cell cancer of the bladder in seven and keratinizing squamous carcinoma of the bladder in one. After intervals of from 0 to 66 mo, each patient was diagnosed as having a second primary tumor originating in the lung. The histology of the lung tumors was oat cell (4), large-cell undifferentiated (1), squamous carcinoma (1), adenocarcinoma (1), and undetermined (1). The appearance of a solitary tumor in the lung of a patient who has been treated in the past for carcinoma of the bladder may not be a metastasis, but rather a new primary carcinoma of the lung. This possibility should be considered, and the patient treated accordingly if a new tumor is confirmed. Although the prognosis for carcinoma of the bronchus is not good, it is better than that for metastasis from carcinoma of the bladder, provided adequate treatment is given. (4 refs)

231. MANAGEMENT OF URINARY BLADDER CANCER.

Fichardt T, Sandison AG
Dept. Radiotherapy, H. F. Verwoerd Hosp., Pretoria, S. Africa
S Afr Med J; 54(18):731-740 1978

From 1960 to 1976, 231 patients (198 men, 33 women) with primary cancer of the bladder were referred to a South African Hospital, and the etiology and clinicopathology of this disease are surveyed based on analyses of these patients and the literature. There were 115 transitional cell carcinomas, 87 anaplastic carcinomas, 15 squamous cell carcinomas, 12 papillary carcinomas, and 2 adenocarcinomas among the study group. Most (90%) of the patients presented with hematuria alone; the others presented with hematuria plus frequency and dysuria, incontinence, and bladder calculi. The duration of symptoms ranged from 2 wk to 2 yr, but most lasted 3-6 mo before diagnosis. The lesions were mostly single, situated mainly on the lateral and posterior walls and on the trigonum. Predisposing factors are numerous and varied, but cigarette smoking poses the greatest hazard for the general population. Cigarette smoking blocks the normal metabolism of tryptophan, leading to an accumulaton of carcinogenic metabolites of tryptophan in the urine. The basic abnormality is an inability to convert 3-hydroxyanthranilic acid to nicotinamide. Other possible etiologic agents include the aromatic amines used in the dyestuff, rubber, and plastic industries; pesticides, especially those containing napthylamines; dyes used in the manufacture of foods, cosmetics and drugs; bilharziasis; and coffee-drinking. Bladder calculi and bladder papillomas may also predispose to bladder cancer. (53 Refs)

232. PATHOLOGY AS RELATED TO TRYPTOPHAN METABOLITE EXCRETION, OCCUPATIONAL HISTORY, AND SMOKING HABITS IN PATIENTS WITH BLADDER CANCER.

Friedell GH, Burney SW, Bell JR, Soto E
St. Vincent Hosp., Worcester, Mass.
J Natl Cancer Inst; 43(1):303-306 1969

The histological characterization of bladder tumors was similar in 10 patients with abnormal and 39 patients with normal excretion of tryptophan metabolites. There was no significant difference between the histology of bladder tumors in patients exposed to industrial carcinogens and those in patients with no known exposure and between bladder tumors arising in smokers and nonsmokers. Since larger numbers of carcinomas composed, in part or totally, of squamous cells came from the group exposed occupationally to carcinogens and the group of smokers, further studies will try to detect significant differences in histological types of tumors arising in groups exposed to different environmental hazards.

233. SQUAMOUS METAPLASIA AND INVASIVE EPIDERMOID CARCINOMA OF BLADDER.

Walts AE
Div. Anatomic Pathology, Cedar-Sinai Medical Center,
8700 Beverly Blvd., Los Angeles, CA 90048
Uropathology; 9(3):317-320 1977

A 29-yr-old woman was admitted for evaluation of recurrent irritative dysuria, left flank pain, and recurrent urinary tract infections. Her medical history included a vaginal hysterectomy for epidermoid carcinoma in situ of the cervix and rheumatoid arthritis. A suprapubic mass slightly to the left of the midline was located, with a second fusiform mass extending to the left lateral pelvic wall. Cytoscopic examination revealed a large, necrotic tumor that occupied most of the anterosuperior bladder wall. The patient underwent an extensive pelvic lymphadenectomy, anterior exenteration and cutaneous ureteroileal urinary diversion. At surgery, a tumor was found extending directly into the left obturator fossa. The pathologic report was a large, exophytic, keratinizing epidermoid carcinoma that deeply infiltrated the bladder wall. It is emphasized that there is an increased incidence of bladder neoplasms in cigarette smokers, in patients with chronic urinary infections, and in Caucasian women with carcinoma of the cervix. Epidermoid carcinoma is found more frequently in women. Close follow-up is suggested for young women with dysuria and chronic urinary infections, especially those with a long history of squamous metaplasia and/or leukoplakia. (15 Refs)

234. FAMILIAL TRANSITIONAL CELL CARCINOMA OF THE BLADDER.

McCullough DL, Lamm DL, McLaughlin III AP, Gittes RF
Univ. California Sch. Med., San Diego, CA
J Urol; 113(5):629-635 1975

A family in which transitional cell carcinoma of the bladder was found in 6 of 34 members who lived beyond age 30 is described; possible etiologic factors, including heredity, carcinogen-exposure, immunologic competence, and tryptophan metabolism, are also evaluated. A genealogy involving 185 family members in six generations was created. Medical histories were obtained and documented where possible, and evidence of exposure to carcinogens was recorded. Histological sections showing transitional cell tumors from five patients were examined. No evidence was found of common exposure to carcinogens; 2 of the 6 had no exposure to tobacco. Three cases occurred among brothers in the first generation; two of the second generation patients were sons of one of these brothers. A daughter of another brother was affected. Screening evaluations were performed on the immediate relatives of the second generation brother pair. In this group no additional tumors were found; urinary cytology and urinalysis were normal. Tryptophan metabolism was normal in all family members, including one of the patients who has had continued recurrences of transitional cell carcinoma. Histocompatibility antigen was compatible with the family relationships reported. Immunologic competence was normal in all unaffected family members, except a daughter of the patient with recurring carcinoma who showed impaired lymphocyte reactivity on repeated testing. Although several previous studies attempting to relate bladder cancer to heredity have failed to demonstrate any statistically significant correlation, the transmission of bladder carcinoma in this family is compatible with an autosomal dominate trait. Since the parent generation was unaffected, the authors suggest that either a mutation occurred in one of the parents or that one parent carried the mutation without expressing it. The mutation passed to approximately half of the offspring, with a high incidence of physical expression. The gene may not be entirely specific, as associated malignancies in patients and other carcinomas in unaffected relations occurred in those who might be expected to have inherited the genetic mutation.

235. UROTHELIAL TUMORS AS A SECONDARY AFFECTION.

Scholl H, Narath P
Urologische Abteilung, Landeskrankenhaus, A-8036 Graz, Austria
Z Urol Nephrol; 69(2):123-126 1976

Urological papillomas were identified in 24/1,267 patients 2-12 yr after diagnosis of various urinary tract diseases. The primary involvement included 13 prostate hypertrophies, 4 renal pelvic stones, 3 ureteral stones, 2 tract infections, 1 hypernephroma, and 1 carcinoma of the penis. The secondary involvement included 12 bladder papillomas, 10 bladder carcinomas, and 2 renal pelvic-ureteral papillomas and carcinomas in 18 men and 6 women. Seven lived in large cities, 3 in small towns, and 14 on farms; 9 were smokers and 10 were nonsmokers (the data were absent in 5). During the entire observation period, 18 had urinary tract infections at least once. Proteins, and also Enterococcus and Pyocyaneus, were involved in 15 infections either concurrent with the primary disease or between the primary and secondary involvements. Moreover, 14 of the papillomas were associated with mixed tract infection. Time-to-tumor after the onset of tract infection was less than 1 yr in 7, 2-7 yr in 10, 11-16 yr in 7. This would tend to eliminate iatrogenic complicity. Chronic inflammation and nitrosamine formation from the reaction of nitrate-reducing bacteria and components of stagnant urine are considered carcinogenic cofactors. A link between papilloma formation and prostate hypertrophy was rejected. (17 refs)

C. Occupational Factors and Smoking as Cofactors in Urinary Tract Cancer

236. OCCUPATION AND CANCER OF THE LOWER URINARY TRACT.

Cole P, Hoover R, Friedell GH
Harvard U. Sch. Public Hlth., Boston, Mass.
Cancer; 29(5):1250-1260 1972

This study is designed to estimate the incident risk of bladder cancer as it is associated with specific occupations. Data based on case reports of 461 persons with cancer of the lower urinary tract were compared to case reports of a control group series of 485 persons. The occupational categories for all persons in the test series are defined and adjusted for age and length of employment. Excessive risk patterns are found to exist in five specific occupation areas: 1) dye-stuffs; 2) rubber; 3) leather; 4) paint; and 5) organic chemicals. Data analyses showed that these categories accounted for 7.3/100,000 cases of urinary tract cancer in men of ages between 20-89 years of age and is considered to be significant. In addition, data provided insight into several occupations which had not been previously suspected as being hazardous. Simultaneous inquiry into the role of cigarette smoking as an aspect of occupational risk in cancer of the urinary tract indicated no correlation existed either directly or indirectly among clerical workers.

237. TUMORS OF THE URINARY BLADDER: AN ANALYSIS OF THE OCCUPATIONS OF 1030 PATIENTS IN LEEDS, ENGLAND.

Anthony HM, Thomas GM
Sch. Med., U. Leeds, England
J Natl Cancer Inst; 45(5):879-895 1970

The correlation of occupation and development of tumors of the urinary bladder was investigated in a survey of the whole-life occupational histories of 1,030 workers in Leeds, England, with bladder papillomas or carcinomas. Hospital patients with lung cancer and with nonmalignant diseases served as controls. Data on smoking habits of the bladder cancer patients was also compiled, but no clear association between cigarette smoking and the occurrence of bladder tumors could be established. Excesses of bladder tumor patients compared to nonmalignant patients and non-bladder cancer patients were found for workers in the textile and clothing industry, electrical and electronic workers, engineering workers, and service, sport and recreation workers. Differences in incidence of bladder tumors compared to controls were significant at the 5% level for engineering fitters, engineers, weavers, tailors, and medical workers (mainly nurses). The ratio of textile workers having bladder tumors to controls having bladder tumors was 20:11, and the ratio of clothing workers with tumors to controls with tumors was 19:11. Dye workers were also at risk, with 3 dye workers having bladder cancer. Among clothing workers, tailors and clothes pressers were at especially high risk, the ratio of bladder cancer patients to controls in these 2 occupational categories being 7:0 and 7:2, resp. High risk was usually associated with long-term employment (e.g, employment of more than 20 yr standing). In dye workers, tailors' cutters and hairdressers, tumors appeared at younger ages. The distribution of papillomas and carcinomas in the patients was similar. It was concluded that of the bladder cancer cases observed, the fraction of cancer cases related to occupation may have been in excess of 20%.

238. URINARY TRACT CARCINOMAS IN GAS INDUSTRY EMPLOYEES.

Manz A
Werksarztliche Dienststelle, Hamburger Gas- und Wasserwerke, D-2000 Hamburg 1, Monckebergstr. 8, West Germany
Munch Med Wochenschr; 118(3):65-68 1976

An epidemiological study of mortality in an urban gas and waterworks facility is presented. Approximately 6,000 persons, including 800 females, were involved. Neoplasms were found in 261 males and 25 females. There were 13 primary urinary tract tumors, including 12 in the bladder and 1 in the renal pelvis. These rates are compatible with the cancer statistics of the general population. However, mortality related to certain occupational duties was significantly higher. Urinary tract carcinoma occurred more often in workers exposed to tars or tar-containing vapors. The mean exposure time was 21 yr, latency (time between last exposure and death) 10.4 yr, and age at death 66 yr. The contribution of smoking was equivocal. Urinary tract polyps were frequent. No worker not so exposed was affected. Prophylaxis against aromatic amines is reviewed.

239. MORTALITY OF GASWORKERS-FINAL REPORT OF A PROSPECTIVE STUDY.

Doll R, Vessey MP, Beasley RWR, Buckley AR, Fear EC, Fisher EW, Gammon EJ, Gunn W, Hughes GO, Lee K, Norman-Smith B
Radcliffe Infirmary, Oxford, England
Br J Ind Med; 29(4):394-406 1972

The mortality experience of selected groups of gasworkers employed by four area Gas Boards and observed over a period of 8 yr was described by us in a report in 1965. The present paper adds a further 4 yr data to those previously collected for men having regular exposure in coal carbonizing plants and for men having exposure only to by-products of the gas-making process. To these we have added data relating to men employed by 4 additional area Gas Boards who have been observed over periods of 7 to 8 yr. The new data provide confirmation that exposure to the products of coal carbonization can give rise to cancer of the lung and leave little doubt that the risk of bladder cancer is also increased. Two additional deaths from scrotal cancer have been observed; there is evidently still a need for vigilance if this disease is to be treated at a stage early enough to prevent death. With respect to all these cancers, work as a topman appears to be particularly hazardous. The additional data included in the present report fail to settle the question whether the risk of lung cancer is especially associated with the conditions of work in one particular type of retort house; if there are any differences, however, they are likely to be small. In our original report, a highly significant association between death from bronchitis and exposure to the coal carbonizing process was described. The more recent data for the 4 original Gas Boards offer only limited support to the view that bronchitis is a specific occupational hazard of gasworkers, and the data for the 4 additional Gas Boards provide no further support whatsoever. The explanation for these discrepancies is obscure, but they may be due to the major changes that have been occurring in the industry during the last decade. No evidence was obtained that by-products workers experience any risk of dying as a result of their occupation. (Author abstract) (16 Refs)

240. THE ETIOLOGY OF CANCER OF THE BLADDER.

Oyasu R, Hopp ML
Northwestern U. Med. Sch., Chicago, Ill.
Surg Gynecol Obstet; 138(1):97-108 1974

Numerous agents have been suggested as urinary bladder carcinogens. Epidemiologic studies indicate that workers in the dye, textile, printing, rubber and cable, and plastic industries have an increased risk of developing bladder cancer. These industries use four compounds which have been shown beyond doubt to be bladder carcinogens in man: beta-naphthylamine, 4-aminobiphenyl, 4-nitrobiphenyl, and 4,4'-diaminobiphenyl. The following agents are strongly suspected of being etiologically significant in the development of bladder cancer by the general population: dietary additives, schistosomiasis, abnormal tryptophan metabolism, tobacco smoking, and viruses. Various animal species have been used as experimental models for the study of induction of cancer of the bladder, and substantial progress has been made in the search for bladder carcinogens, etiologic factors, and the pathogenesis of this disease. Although knowledge of the tumorigenesis of the cancer remains limited and fragmentary, it appears certain that multiple agents are responsible for the induction of bladder tumors. Clinicians should watch carefully for continual exposure to possible carcinogens in what appear to be harmless procedures. Cooperative work by oncologists, ecologists, toxicologists, physicians, and those in public health service is urgently needed in the study of urinary bladder tumorigenesis.

241. ETIOLOGY AND PATHOGENESIS OF BLADDER CANCER.

Wolf H, Wagenknecht LV, Madsen PO
175 references
Urologe; 8(2):81-96 1969

In a discussion of bladder cancer epidemiology in man, the roles of certain chemicals often appearing as by-products of some industries (especially beta-naphthylamine), smoking and schistosomiasis are discussed. Methods for inducing bladder cancer in animals, and metabolic pathways of aromatic amines (especially tryptophan), are presented. A brief discussion of the possible causes of localized outbreaks of bladder cancer in cattle is also included.

242. PROBLEMS OF OCCUPATIONALLY RELATED LUNG CANCER. LONG-TERM OBSERVATIONS IN THE BASF (BADISCHE ANILINE AND SODA MANUFACTURING COMPANY).

Oettel H, Thiess AM, Uhl C
Badischen Anilin and Soda-Fabrik AG, Ludwigshafen-/Rhine, Germany
Zentralbl Arbeitsmed; 18(10):291-303 1968

From 1912-1967 (inclusive), lung cancer was found in 373 male employees (and 1 female employee) of this chemical factory. The incidence remained fairly stable until 1950, then rose sharply; 260/373 cases were seen in 1957-1967 (inclusive). The lung cancer incidence/av number of male employees at any given time was 5/24,400 in 1936-1940, 134/40,370 in 1961-1965, 21/41,220 in 1966 and 21/40,700 in 1967. The absolute number of cases fell somewhat in 1966 and 1967, but 150 cases are expected for the next 5-yr period. The marked increase in lung cancer after 1950 coincided with an increase in the reported incidence of smoking (no other details). Peak ages in the lung cancer patient group were 55-65 yr; the only patient under 41 was a moderate smoker, employed for about 1 yr and exposed to highly toxic borane compounds. The lung cancer incidence, tabulated according to occupation in the 259 patients seen from 1957-1967 (inclusive), was 138-158/10,000 similarly employed persons in 2 groups (mechanics and transportation workers) and 31.8-56.5 in 3 other groups; the only significantly increased incidence was seen in insulation workers (7/171 insulation workers = 410/10,000). These 7 men were smokers; only 1/7 showed asbestos is, and none of the tumors was identified as a mesothelioma. Occupational risks of bladder cancer are also briefly discussed: of the 102 cases seen in Ludwigshafen in 1895-1958, 74 were traceable to known bladder carcinogens beta-naphthylamine in 71/74, diaminodiphenyl in 3/74), and at least 25 others to suspected bladder carcinogens (including anilines). A connection between bladder cancer and smoking was suspected.

243. AROMATIC AMINES: THE PRESENT STATUS OF THE PROBLEM.

Veys CA
British Rubber Manufacturers' Assoc., Birmingham
Ann Occup Hyg; 15:11-15 1972

Data on the occupational hazards associated with aromatic amines, potent bladder carcinogens, are reviewed. The eight occupational categories in which increased bladder cancer incidence may be related to aromatic amine exposure are chemical and dyestuff industries; textile dyeing and printing; pigment manufacturer; rubber and cable making; gas workers; laboratory workers; rodent control; and patent fuel, tar and pitch workers. As yet no safe exposure level has been established for aromatic amines. Two aromatic amines alpha-naphthylamine and beta-naphthylamine are released by curing tobacco, and may cause the observed high incidence of bladder cancer in heavy cigarette smokers. Three carcinogenic aromatic amines that may present risks for laboratory and chemical workers are benzidine, o-tolidine and o-dianisidine. A report from the United States indicated an apparent excess of deaths from cancer of the pancreas and malignant lymphoma in members of the American Chemical Society, but surprisingly few cases of urinary bladder cancer. In Britain, there has been no purposeful survey of bladder tumor incidence among aromatic amine-exposed chemical and laboratory workers.

244. EPIDEMIOLOGY OF BLADDER CANCER. (PP. 65-86)

Clayson DB
The Biology and Clinical Management of Bladder Cancer. Cooper EH, Williams RE, ed. London, Blackwell Scientific Publications, 1975.

The epidemiology of bladder cancer, including problems of individuality and the reliability of mortality and morbidity data, is discussed. The difficulty in drawing valid conclusions about bladder tumors from large numbers of individuals stems from the fact that individuals differ in their inherited characteristics and in their exposure to environmental factors. Despite serious reservations about the accuracy of national and regional cancer statistics, it is possible to draw broadly based conclusions, eg, age-adjusted mortality rates for bladder cancer in males in white South Africa, Denmark, Sweden, and Japan; and bladder tumors are more frequent in males than females. Epidemiologic studies indicate that the incidence of bladder cancer is two to three times higher in male cigarette smokers than in nonsmokers. Experimental evidence for an association between smoking and bladder cancer is lacking, but tobacco smoke contains minute traces of a potent human bladder carcinogen, 2-naphthylamine. Bladder cancer is also caused by exposure to aromatic amines (2-naphthylamine, 1-naphthylamine, benzidine, and 4-aminobiphenyl), mainly in the chemical and rubber industries. The latent period between entry into work with an occupational carcinogen and development of bladder cancer is lengthy (18-22 yr). Men who have been exposed to these carcinogens are advised to have urinary cytologic tests carried out at intervals not exceeding 6 mo. Other occupations suspected of being at increased risk for bladder cancer include hairdressers, possibly due to dyestuffs, nurses, perhaps because of the former use of benzidine in the classic test for occult blood in feces or urine, and leatherworkers. Other epidemiologic studies suggest a connection between bladder cancer and the drug, chlornaphazin, and between bladder cancer and coffee drinking, probably as a result of caffeine which is mutagenic in lower organisms. (65 refs)

245. AN EPIDEMIOLOGICAL INVESTIGATION OF CANCER OF THE BLADDER.

Wynder EL, Onderdonk J, Mantel N
Sloan-Kettering Inst. Cancer Res., New York
Cancer; 16(11):1388-1407 1963

After a review of the literature (50 refs) in which it is noted that information on bladder cancer is incomplete as to some areas of the world and as to occupation groups, a study by interview was made of 300 male and 70 female bladder patients in several New York City hospitals; matched controls were selected from the hospital population excluding those with cancer of the lung, upper GI tract or with myocardial infarction. The disease is predominantly male and is increasing in some countries. A high correlation with cigarette smoking was confirmed, especially in those who smoke more than 20 per day. As to occupation, while the higher risk in aniline dye workers is well known, other occupations appear to have an increased risk, especially shoe repairers and leather workers. Also under suspicion are painting, hairdressing, certain textile operations, coal mining, and perhaps plumbing. There appears to be a positive association between bladder stones and bladder cancer. There are a variety of factors that do not seem to play roles in bladder cancer, including family history, alcohol consumption, intake of liquids, diet, and diseases other than bladder stones. Most excess cases of bladder cancer among males may be assumed to have exogenous causes.

246. CANCER RISKS ASSOCIATED WITH EMPLOYMENT IN THE LEATHER AND LEATHER PRODUCTS INDUSTRY.

DeCoufle P
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20014
Arch Environ Health; 34(1):33-37 1979

A recent study of relationships between occupation and cancer at Roswell Park Memorial Institute, Buffalo, New York, identified significantly high risks of bladder cancer among men and women with a history of employment in plants manufacturing leather and leather products. Eleven men and four women with bladder cancer had been employed between 1956 and 1965 in these plants, and their relative risks were estimated to be 6 and 4 times those of clerical workers, respectively. Among the men, the relative risk increased with duration of employment and remained elevated after adjustment for smoking habits. Male leatherworkers also had significantly increased risks for cancers of the buccal cavity and pharynx and larynx that could not be explained by differences in smoking habits. Malignant lymphomas were also associated with elevated risks among men and women who had worked in the leather industry. A review of processes and agents found in leather manufacture revealed several steps that involved exposure to potentially carcinogenic materials, including tannin extracts and tannic acid plus azo and other synthetic dyes, that have induced cancer in laboratory animals. There should be further studies of persons employed in the leathermaking and fabrication industries to characterize the nature of exposure-response relationships. (30 Refs)

247. RATES, INTERVIEW, AND PATHOLOGY STUDY OF CANCER OF THE URINARY BLADDER IN NEW ORLEANS, LOUISIANA.

Dunham LJ, Rabson AS, Stewart HL, Frank AS, Young JL
NCI, Bethesda, Md.
J Natl Cancer Inst; 41(3):683-709 1968

From 1958-64, 702 new cases of presumptive or confirmed primary bladder cancer were identified and 631 were histologically confirmed as transitional cell (92%), squamous cell (4.3%), undifferentiated (1.7%) carcinoma, adenocarcinoma (1.1%), sarcoma (0.6%) and unclassified types (0.3%). New Orleans residents (St. Bernard, Orleans and Jefferson parishes; 564 patients) were selected for the incidence study. Of the 631 patients, 337 were white males, 78 Negro males, 167 white females and 49 Negro females; age-adjusted incidence rates/100,000/yr were 19.0, 11.2, 7.4 and 7.2, resp. (total 11.4). Transitional cell carcinoma was less frequent in the Negro patients (88.5% in males, 67.5% in females) but squamous cell carcinoma was higher (7.6% and 18.3%, resp); adenocarcinoma and undifferentiated carcinoma were higher in Negro females (each 6.1%), than in white patients The incidence rates varied from 1 yr to another; the total incidence was about 30% lower than the 21.1/100,000 reported for New Orleans in 1947. Excessive occupational risks in white males included sailors and deckhands, tinsmiths and coppersmiths, machinists, civil engineers, plumbers, structural metal workers, barbers and carpenters. A significant correlation between tobacco use (all forms combined) and bladder cancer was seen in males only.

248. EPIDEMIOLOGY OF CANCER OF THE BREAST, STOMACH, ESOPHAGUS, LUNGS, BLADDER AND HODGKINS DISEASE.

Heyden S
Duke U. Med. Ctr., Durham, N. C.
Dtsch Med J; 20(1):3-9 1969

This is a review and discussion. Every factor which contributes to lowering of estrogen levels decreases the risk of breast cancer in women. In Japan where women have many children and usually nurse them for long periods of time the incidence of breast cancer is one-ninth that in the West. The extremely high incidence of stomach cancer in Tyrol (Austria) and Poland is attributed to consumption of large quantities of lard, the high incidence in Japan (fat-poor diet) to malignant transformation of stomach ulcers which are common in that country. Different etiologic factors are responsible for tumors in different segments of the same organ (for instance uterine cervix and corpus cancer): high incidence of esophagus carcinoma (upper third of the esophagus) in Sweden was attributed to a lack of iron and sideropenia, while the extremely frequent esophagus cancer among the Bantu in South Africa who have a very high blood iron level, is localized in the thoracal part of the esophagus. Different histology of neoplasms in the same organs can also be an expression of different etiologic factors. The dependence of cancer of the bladder on occupational factors is well established, but smoking also seems to be a causative factor. Hodgkins disease is almost unknown in people less than 50 yr old in Japan, but in older age groups its frequency is as high as in Europe or the USA.

249. THE CAUSES OF URINARY BLADDER CANCER AS EVALUATED IN AN EPIDEMIOLOGIC STUDY.

Pryanichnikova MB
Clinic Faculty Surgery, Kuibyshev Medical Inst., USSR
Urol Nefrol (Mosk); (6):28-31 1977

To evaluate the high-risk exogenous and endogenous factors for cancer of the urinary bladder, 250 patients with urinary bladder cancer (group 1), 100 patients with urinary bladder papillomas (group 2) and 506 practically healthy controls underwent a retrospective epidemiological survey. The incidence of both carcinoma and papilloma of the urinary bladder was the highest among the individuals who had occupational exposure to oil-products (53% compared to 20.9% in the controls). Smoking and alcohol consumption were recorded in 68.8% and 82.8% of the patients, compared to 54.0% and 67.5% of the controls. Hereditary predisposition to the urinary bladder neoplasms was detected in 15.6% of the patients and only in 8.8% of the controls. (5 Refs)

250. AN INQUIRY INTO THE LIVING HABITS OF THE PATIENT WITH BLADDER TUMOR.

Tedeschi LG, Jackson DR, Barber DE
Boston U. Med. Ctr., Mass.
Boston Med Q; 14(2):52-56 1963

An inquiry into the living habits of 206 patients with histologically proven bladder malignancies disclosed potential hazards inherent to employment in 36 (17.9%); of these only 1 had been involved in the manufacture of 2-naphthylamine. A family history of bladder tumors was elicited in 20 cases, 6 in brothers and 4 in fathers. Tumors in other parts of the body had been present in 37 (17.9%), and a history of urinary infections was reported by 16.4%. Information concerning non-industrial, common environmental agents (including drinking and dietary habits), and intake of arsenicals and other therapeutic agents failed to reveal any strong trend. Among the patients were 140 (68%) present smokers and 14.5% past smokers, suggesting either the presence of a potential urinary bladder carcinogen in products of cigarette smoke, or stimulation from smoking of metabolic processes leading to synthesis of endogenous urinary bladder carcinogens. In this series the sex ratio was 160 males to 46 females, with 55% of the tumors in decade 6, 22% in decade 5, and 8% in decade 4.

251. URINARY BLADDER CANCER: POTENTIALS OF AND PROBLEMS ASSOCIATED WITH EARLY INTERVENTION STRATEGIES.

Bryan GT
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Semin Oncol; 6(2):161-165 1979

Early intervention strategies in bladder cancer (BC) are reviewed. Because a disease state can be divided pathogenetically into identifiable stages, attempts to alter the course of the disease by modifying one of these stages are attractive intervention strategies. To form a clinically detectable neoplasm (approx 1 cm3, 10(9) cells), a neoplastic cell and its progeny must undergo about 30 cell divisions; only about 7 more divisions are required to form a lethal mass. Hence, prevention and intervention strategies must occur before a detectable tumor exists. Since the av age at diagnosis of BL is 68 yr in the US, it is imperative to identify those individuals at increased risk. Recognized risk factors include age, sex, occupation, and smoking habits; possible risk factors are prior pelvic irradiation and consumption of coffee or artificial sweeteners. One intervention strategy adds an agent or agents to the environment of an individual to interfere with hypothetical bladder carcinogenic mechanisms. These additives have one of three modes of action: (1) interference with carcinogen-target interaction (eg, beta-glucuronidase inhibition, free-radical scavenger agents), (2) alteration of the molecular balance between activation and detoxication toward detoxication (eg, detoxication enzyme induction, inhibition of activation enzymes, addition of cofactors to inhibit carcinogen or promoter formation), and (3) inhibition of the growth and development of initiated cells by retinoids, protease inhibitors, etc. The effectiveness of these methods to date, largely not spectacular, is summarized. (28 Refs)

252. AN EPIDEMIOLOGICAL STUDY OF BLADDER CANCER (MEETING ABSTRACT).

Howe GR, Chambers L, Gordon P, Morrison B, Miller AB
Natl. Cancer Inst. Canada, Memorial Univ. Newfoundland, St. John's, Newfoundland, Canada
Am J Epidemiol; 106(3):239 1977

A case-control study was conducted in three Canadian provinces using 532 cases of bladder cancer and an equal number of controls individually matched on age, sex, and neighborhood of residence. Increased risk was associated with an occupational history in the chemical, rubber, photographic, petroleum and food processing industries for males, and also with medically related occupations, though for some the numbers exposed were too small to attain statistical significance. Exposure to dust and fumes in other industries was a risk factor for both males and females and in specific occupations, including crop spraying, welding, occupations involving exposure to diesel and traffic fumes, metal machining and barbers. Use of hair dyes was significantly increased among male cases, though exposure was in nearly all cases limited to 5 yr before diagnosis. Use of a nonpublic water supply at any time was a highly significant risk factor for males. A strong association with cigarette smoking was seen for both sexes. A highly significant risk from drinking instant coffee was observed for both males and females, though for the latter, most of the association seems due to confounding by smoking. (Author abstract) (no Refs)

253. THE ETIOLOGY OF BLADDER CANCER FROM THE EPIDEMIOLOGICAL VIEWPOINT.

Miller AB
Epidemiology Unit, Natl. Cancer Inst. Canada, Univ. Toronto, 121 St. Joseph St., Toronto, Ontario, M5S 2R9, Canada
Cancer Res; 37(8,part2):2939-2942 1977

A number of causal environmental factors have been identified for bladder cancer. Quantification of the extent to which known and suspect factors account for the cases that occur is one of the current goals of research in bladder cancer epidemiology. Certain occupational groups have been identified for which a clearly increased risk has been demonstrated; smoking has also been demonstrated as a risk factor. Of the residual, due to presently unknown factors, it has been pointed out that possibly as much as one-half of the men and maybe two-thirds of the women could be accounted for by coffee drinking. Preliminary analysis of a case-control study conducted in Canada has confirmed the importance of cigarette smoking in both sexes, and has indicated a slightly increased risk due to consumption of regular coffee in males and due to heavy use of instant coffee in both sexes. These risks are only partially accounted for by an association between smoking and coffee drinking. Although possibly most of the risk factors have been identified for bladder cancer in men, in women it still seems likely that a number of substances to which the general population is exposed may be found to be carcinogenic to the bladder. (Author abstract) (12 Refs)

254. THE EPIDEMIOLOGY OF BLADDER CANCER. A SECOND LOOK.

Wynder EL, Goldsmith R
American Health Foundation, 1370 Ave. of the Americas, New York, NY 10019
Cancer; 40(3):1246-1268 1977

The epidemiology of bladder cancer is considered based on a case-control study of 574 men and 158 women seen over a 5-yr period, and these results are compared to those from previous investigations. Bladder cancer occurs more in men than in women, except in Egypt, where both sexes are exposed to Schistosoma hematobium and the incidence is about equal. Bladder cancer also affects nearly twice as many white men and women as black women. Cigarette smokers of both sexes were at a higher risk than nonsmokers. About 50% of the male cases and 33% of the female cases were attributed to cigarette smoking; there was a fairly consistent dose-response relationship for amount and duration of smoking in both sexes. However, no significant differences were observed between the proportions of cases and controls who used pipes, cigars, chewing tobacco or snuff. There was also an excess of bladder cancer in persons with occupational exposure to rubber, chemicals and textiles. An increase in risk with coffee drinking was noted in both sexes; this increase was slightly higher in men and was independent of smoking levels. No relationship was found between alcohol consumption and bladder cancer. No association was found for artificial sweeteners. It is suggested that further studies concentrate on metabolic factors since cigarette smoking and occupational exposure did account fully for the observed incidence. (120 Refs)

255. A POPULATION-BASED STUDY OF BLADDER CANCER.

Cole P
Host Environment Interactions in the Etiology of Cancer in Man Proceedings of a meeting held at Primosten, Yugoslavia, 27 August-2 September 1972. International Agency for Research on Cancer , Lyon, France, 1973.

The proportion of bladder cancer cases in a representative population that could be attributed to smoking and occupation was assessed, and other possible hazards were considered. The author made a case-control study of a total incidence series of lower urinary tract cancers (92% had bladder tumors). Controls were age- and sex-matched but otherwise randomly selected; 470 cases and 500 controls were interviewed. The population attributable risk percent (AR%) was calculated for the variables of smoking, hazardous occupation, and coffee drinking. (The AR% is that proportion of the disease that is caused by a specific exposure, assuming a causal relationship). With respect to bladder cancer and smoking, the AR% for men was 35%. An estimate is not given for women because bladder cancer is characteristically a disease of advanced age, and women did not take up cigarette smoking to any appreciable extent until 1920. The number of female smokers is increasing, however, and, undoubtedly, so will the AR%. The occupational AR% is estimated to be 18% among men, reflecting differing occupational experiences, but the figure varies between populations. However, even among men in industrialized societies, probably not more than 25% of the disease can be attributed to occupational exposures. With respect to coffee drinking, the author concludes that it remains to be determined whether a consistent association exists with risk of disease; then detailed analyses of the AR% will be warranted.

256. PUBLIC HEALTH VALUE OF USING EPIDEMIOLOGIC INFORMATION TO IDENTIFY HIGH-RISK GROUPS FOR BLADDER CANCER SCREENING.

Morrison AS
Dept. Epidemiology, Harvard Sch. Public Health, Boston, MA, 02115
Semin Oncol; 6(2):184-188 1979

The public health value of using known bladder cancer risk factors (eg cigarette smoking, pelvic irradiation, etc) to screen high-risk groups for this disease is assessed. Bladder cancer data in the United States between 1969-1971 show that for both sexes, and races (white/black), incidence rises sharply with age; the age-standardized incidence is about 2.5 times greater for men than for women. Workers exposed to a small group of aromatic hydrocarbon dyestuff intermediates have a risk 30 times that of unexposed individuals. The elevated bladder cancer risk found in 1/4 of the men in a Boston area study, who had worked in 5 occupational categories, was attributed to their work histories. The rate was 1.8 times that among unexposed men; occupational exposure accounted for about 1/5 of the cases. Seventy-three percent of the men in this study had smoking histories, and cigarette smoking accounted for about 40% of bladder cases. The ability of a risk factor to identify those with the detectable preclinical place (DPCP) of the disease is the factor's sensitivity. It is defined as the proportion of those cases with DPCP who have the factor. The specificity of a factor is defined as the proportion of those who have neither the DPCP, nor the factor. The practical difficulty in estimating sensitivity and the feasibility of screening methods are discussed. (7 Refs)

257. RELATIVE IMPORTANCE OF RISK FACTORS IN BLADDER CARCINOGENESIS.

Miller CT, Neutel CI, Nair RC, Marrett LD, Last JM, Collins WE
Health Protection Branch, Health and Welfare Canada, Ottawa, Canada
J Chronic Dis; 31(1):51-56 1978

Responses from outpatients with urological complaints were recorded in a detailed questionnaire exploring potential risk factors in bladder cancer. The subjects were subsequently classified on the basis of hospital records as cancer cases or controls. Each of the 265 cases was matched to 2 controls of the same age and sex. History and treatment of tuberculosis of all subjects were verified through the four geographically adjacent tuberculosis registers. Analysis of exposures of matched triples revealed six statistically significant associations with bladder cancer in men smoking, gout, allergies (self), allergies (family), occupational radiation exposure, and occupational exposure to chemicals. In women, there was one significant positive association (coffee consumption) and one significant negative association (allergies, self). Although the relative risk of isonicotinic acid hydrazide (INH) exposure in women was the highest observed (3.0), the number of exposured individuals was too small to permit any meaningful conclusion. Discriminant analysis was used to rank the variables in order of their importance as potential risk factors. Statistically significant ability to discriminate cases from controls was observed in men for (1) allergy (family), (2) occupational exposure to radiation, (3) occupational exposure to chemicals, and (4) smoking. In women, the significant discriminators were (1) coffee consumption, (2) history of tuberculosis and INH treatment, and (3) allergy (self, protective effect). The suggestion that INH is a potential carcinogen indicates that further study of the association of the drug with bladder cancer is in order. (23 Refs)

258. RADIUMHEMMET: A WORLD CENTER FOR BLADDER CANCER.

Oesterberg S
No affiliation given
Lakartidningen; 73(19):1788 1976

General epidemiologic, etiologic, diagnostic, and therapeutic problems of urinary bladder cancer are discussed. Bladder cancer accounts for 5% of all cancers in men, but its incidence among women is lower. Different hydrocarbons encountered in the petroleum, asphalt and rubber industries, coffee and tobacco are suspected as etiologic factors of bladder cancer in industrialized countries. Schistosomiasis is a major factor in bladder cancer in Egypt. Oncofetal and carcinoembryonal antigens are of diagnostic value. Treatment consists of ionizing radiation, chemotherapy, surgery, and their combinations. (no refs)

259. LOWER URINARY TRACT. (PP. 233-262)

Cole P
Cancer Epidemiology And Prevention Current Concepts. Schottenfeld D, ed. Springfield, Charles C Thomas, 1975.

Each year 21,000 Americans develop cancer of the lower urinary tract (renal pelvis, ureter, bladder, urethra). Initially, tumors of the lower urinary tract appear benign, but they may recur and metastasize. The little epidemiological data available show moderate international variation with somewhat higher rates for industrialized areas. Incidence rates show divergent trends for men, women, whites, and blacks that are not readily explainable. Marital status, religion, nativity, urban-rural domicile, and social class data also show variation in cancer mortality. Exposure to 2-naphthylamine and other aromatic amines used in dyestuffs has been the only strong and consistent causal link to the disease. Cigarette smoking, aberrations in tryptophan metabolism, and infection with Schistosoma haematobium have been suggested as etiologic factors, but the evidence is inconclusive. Other suspected causes include: pelvic irradiation, artificial sweeteners, coffee drinking, ingestion of bracken fern, analgesic abuse, urine stasis, or viruses. Some data suggest a different etiologic pattern in different age-sex groups. (121 refs)

260. EPIDEMIOLOGY OF CANCER OF THE RENAL PELVIS AND URETER.

Schmauz R, Cole P
Med. Sch., Lubeck, W. Germany
J Natl Cancer Inst; 52(5):1431-1434 1974

Forty-three persons with cancer of the renal pelvis or ureter were compared with 509 persons with cancer of the bladder and with controls drawn from the population of the study area. Data were gathered by at-home interviews. Cancers of all three sites occur predominantly in men and in old age. Increased risk of bladder cancer is associated with low exposure to cigarette smoking, coffee drinking, and leather work. For cancers of the renal pelvis and ureter, excess risk is found only for high levels of exposure. The rapid transit of carcinogens through the renal pelvis and ureter may explain the association of cancer at these sites with only high-level exposures. Population attributable risks (i.e. the proportion of the disease that could be prevented if the exposure studied were a cause and if it were stopped) were computed for each exposure. It is estimated that 38.8% of the cases of cancer of the renal pelvis and ureter in men is attributable to cigarette smoking, 45.0% to coffee drinking, and 4.7% of the cases in men and women to the occupation of leather working. The values for bladder cancer are 41.0, 26.6, and 2.4%, resp.

261. EPIDEMIOLOGY OF ADENOCARCINOMA OF THE KIDNEY.

Wynder EL, Mabuchi K, Whitmore WF
American Hlth. Fdn., New York, N. Y.
J Natl Cancer Inst; 53(6):1619-1634 1974

Etiologic factors of adenocarcinoma of the kidney were identified through a literature review and a case-control study. The case-control study was conducted on 202 patients (129 men and 73 women) with renal adenocarcinoma and 394 controls matched for sex, age, race, and hospital. The study showed a significant but moderate association between cigarette smoking and renal adenocarcinoma; the overall relative risk for cigarette smokers was 2.0 in males and 1.5 females. Relative risks increased with an increase in the number of cigarettes smoked/day and were greater for males less than 50 yr of age than for those over 50 yr. Male cases indicated a significantly larger proportion of persons with a history of myocardial infarction (7%) than did controls (1%). Female cases contained a greater proportion of obese (at least 25% overweight) persons (28.8%) than did their controls (10.1%). Female renal adenocarcinoma cases included a smaller percentage of individuals who had never married than their controls; no differences were found related to reproductive variables such as parity. No significant relationships with coffee drinking, alcohol consumption, or occupational exposure could be determined. As a working hypothesis from this data, it is suggested tha dietary factors, possibly related to a fat and/or cholesterol intake, are involved in the pathogenesis of renal adenocarcinoma.

262. FAMILIAL URINARY BLADDER CANCER.

Purtilo DT, McCarthy B, Yang JP, Friedell GH
Department Pathology, University Massachusetts Medical School, Worcester, MA
Semin Oncol; 6(2):254-256 1979

The clinical and pathological features of 13 cases of bladder transitional cell carcinoma (TCC) in 6 unrelated families in the Worcester, Massachusetts area illustrate the contention that genetic factors may play an important role in the etiology of bladder TCC. The affected individuals were two male siblings (aged 62 and 55 yr) in family 1, two male siblings (aged 59 and 56 yr) in family 2, brother and sister (aged 91 and 89 yr) in family 3, two male siblings (aged 39 and 52 yr) and family 4, two brothers and a daughter of the first brother (aged 33, 28, and 19 yr) in family 5, and a father and son (aged 73 and 62) in family 6. Occupational and smoking habit risks were prevalent in all these patients except those in family 3, the 52-yr-old patient in family 4, and the 19-yr-old patient in family 5. These cases of TCC displayed the major features of familial cancer: 1) affected individuals were younger than the usual non-familial cases; 2) multiple TCC with frequent recurrences and multiple genitourinary carcinomas occurred in families 3 and 4; 3) there was general concordance in types of cancer; and 4) there was concordance of age at time of appearance of TCC in siblings. The pattern of inheritance in families 5 and 6 suggests a Mendelian autosomal dominant trait. The possibility that an inherited predisposition to bladder TCC or a heightened susceptibility to environmental carcinogens operates in familial cases of bladder TCC is discussed. (18 Refs)

D. Artificial Sweeteners, Coffee Drinking and Smoking as Cofactors in Urinary Tract Cancer

EDITOR'S NOTE: Additional studies, dealing with both coffee drinking and occupational factors, may be found in the preceding category, "Occupational Factors and Smoking as Cofactors in Urinary Tract Cancer."

263. BLADDER CANCER: SMOKING, BEVERAGES AND ARTIFICIAL SWEETENERS.

Morgan RW, Jain MG
Dept. Preventive Medicine, Sch. Hygiene, Univ. Toronto, Toronto, Ontario M5S 1A1, Canada
Can Med Assoc J; 3:1067-1070 1974

A matched patient-control study of bladder cancer examined the relationship of the disease to occupation, smoking and intake of tea, coffee, cola, alcohol and artificial sweeteners. There was no association of disease with occupation for these patients. Heavy smoking gave relative risks of 6.37 and 4.36 for men and women respectively; there was evidence of a dose-response relationship. Tea and coffee intake did not increase the risk of disease nor did prolonged use of artificial sweeteners. Alcohol and cola intake increased the relative risk of bladder cancer among male smokers. There is some suggestion that smoking interacts with both alcohol and cola intake in the production of bladder cancer. (Author abstract) (22 Refs)

264. SACCHARIN, CYCLAMATE, AND HUMAN BLADDER CANCER. NO EVIDENCE OF AN ASSOCIATION.

Kessler II, Clark JP
Dept. Epidemiology and Preventive Medicine, Univ. Maryland Sch. Medicine, 655 W. Baltimore St., Baltimore, MD, 21201
JAMA; 240(4):349-355 1978

The results of a hospital-based case-control study of the possible roles of saccharine and cyclamate in human urinary bladder cancer are reported. The study groups consisted of 519 patients with histopathologically confirmed bladder cancer and 519 matched controls (cancer-free patients) from metropolitan Baltimore. All subjects were subjected to an intensive personal interview with respect to smoking habits, occupational history, and use of nonnutritive sweeteners (NNS). The proportions of patients and controls who ever used NNS in any form were the same (39.5%), and the frequency, quantity, or duration of intake of these substances did not differ significantly between the two groups. These normal findings persisted after simultaneous adjustment for the effects of smoking, occupation, age, diabetes mellitus, and several other potentially confounding factors. The failure of the relative risk of bladder cancer to increase with increasing NNS exposure is also inconsistent with an etiologic relationship. However, cyclamates were introduced too recently to permit the detection of carcinogenic effects appearing more than 10 or 15 yr after initial exposure. It is concluded that neither saccharin nor cyclamate is likely to be carcinogenic in man, at least at the moderate dietary levels reported by the patient sample. (18 Refs)

265. SYNTHETIC SWEETENER CONSUMPTION AND BLADDER CANCER TRENDS IN THE UNITED STATES.

Burbank F, Fraumeni JF
NCI, Bethesda, Md.
Nature (Lond); 227(5255):296-297 1970

In a study of the general use of cyclamates and the toxicity of artificial sweeteners, the U.S. Department of Health, Education and Welfare found no clear-cut separation in age-specific or age-adjusted mortality rates for bladder cancer from 1950-1967, inclusive (1962 being the yr cyclamate consumption dramatically increased). Incidence rates for bladder cancer showed only a long-term increase in rate (by about 8/100,000 over the 17-yr period) which may be related to cigarette smoking. As yet, bladder cancer rates do not appear affected by synthetic sweeteners, but the time period is considered too short and the dosage too low for examples of cyclamate carcinogenicity to have appeared. Chromosome breaks in vivo in rats and in vitro in human cells due to cyclamates and cyclohexylamine are also mentioned.

266. SACCHARIN PLUS CIGARETTES TIED TO BLADDER CANCER IN MEN.

Anonymous
No affiliation given
Med World; 20(11):10-11 1979

The possibility that not saccharin (SC) alone but SC plus cigarette smoking increases the risk of bladder cancer (BlC) in men has emerged from a dispute over new and old interpretations of old epidemiological data. The author of a study of 260 men and 86 women with BlC and 2,235 men and 1,602 women without BlC had initially concluded that there was no association between SC use and BlC. However, the author's second look at his data showed that the cancer risk was almost triple for men who consumed SC and were also moderate cigarette smokers. This reversal, which was sent to the National Cancer Institute in November 1977, took 18 mo to surface. (no Refs)

267. BLADDER CANCER MORTALITY IN ENGLAND AND WALES IN RELATION TO CIGARETTE SMOKING AND SACCHARIN CONSUMPTION.

Armstrong B, Doll R
Radcliffe Infirm., Oxford, England
Br J Prev Soc Med; 28(4):233-240 1974

Cohort analyses of bladder cancer mortality in men and women in England and Wales were compared with figures for the per capita consumption of saccharin and cigarette tobacco and with similar analyses of cigarette smoking habits. That increases in bladder cancer mortality in men are due to cigarette smoking is supported by the correspondence between the first male cohorts to show a sharp increase in mortality (those born around 1865-1875) and the beginning of significant cigarette smoking by men (1890, when these cohorts had a mean age of 15-25 yr); and by the correspondence between the male cohort with peak bladder cancer mortality (that born around 1900) and that with the maximum percentage of cigarette smokers. In women, there are no clear increases in bladder cancer mortality corresponding to the mass increase in cigarette consumption starting in 1920. Trends in bladder cancer mortality in men and women show no evidence of any break in continuity that could be attributed to the use of saccharin since 1939. However, it may be to early to see an effect of saccharin consumption on mortality rates.

268. BLADDER CANCER AND SACCHARIN.

Anonymous
No affiliation given
Lancet; 2(8038):592-593 1977

Recent studies suggesting that there is a positive relationship between artificial sweeteners (AS) and the risk of bladder cancer are critically reviewed. Examination of bladder cancer mortality rates in Britain and the United States revealed no increase attributable to saccharin consumption. Diabetics in both these countries do not exhibit a higher incidence of bladder cancer. A direct postal questionnaire sent to 364 patients (240 men) with bladder cancer and 470 control patients with benign prostatic hypertrophy (310) or stress incontinence (160 women) revealed no positive relationship between AS consumption and cancer incidence. No difference in the intake of AS was found between a group of 209 patients (157 men) with bladder cancer and a group of matched controls. In one study, 632 patients (480 men), (from three Canadian provinces) with recently diagnosed bladder cancer were questioned about their consumption of saccharin, coffee, and tobacco. Significantly more men with bladder cancer reported having used AS than did controls, and it was concluded that AS causes bladder cancer in men. The conclusions overlooked the fact that the women with cancer used less AS than their controls and that, when results from both sexes are combined no significant relationship is found. The possibility that the association might reflect an indirect association (such as that of coffee and tobacco consumption) was not investigated. Cigarette consumption was studied only by dividing the men into those with a lifetime cigarette consumption below or above 10,000 packs, and coffee consumption was studied by asking whether instant coffee was 'ever consumed' or 'never consumed.' Other types of coffee were not considered. Other biases can be found in the Canadian study. A recent careful study using 146 cases and 132 matched controls showed that the risk of cancer in AS users of either sex is, if anything, lower than in non-users. It is concluded that further work on the relationship between bladder cancer and AS consumption is needed. (19 Refs)

269. CANCER MORTALITY IN RELATION TO NATIONAL CONSUMPTION OF CIGARETTES, SOLID FUEL, TEA, AND COFFEE.

Stocks P
Colwyn Bay, Wales
Br J Cancer; 24(2):215-225 1970

Age-adjusted death rates from cancers of varying sites in 1964-1965 were compared to figures for annual consumption of cigarettes, solid fuel, tea, and coffee collected from trade statistics in 20 countries. One significant correlation found was that cigarette consumption per adult in the population is positively related with lung and bladder cancer in males and insignificantly with lung cancer in females. Negative relations are indicated with the liver and biliary passages, prostate and uterus. Solid fuel is positively related with the intestine, lung and bladder in both sexes, with leukemia in males and with breast in females; however, negative associations are indicated with the stomach. Tea is positively related with intestine except rectum in both sexes and with larynx, lung and breast in females. Negative associations are indicated with the stomach in both sexes and with uterus and leukemia in females. Coffee is positively related with the pancreas, prostate and leukemia in males and with ovary and leukemia in females. The contrasts observed between the intestine and stomach in their associations with solid fuel, cigarettes and tea may be explained by the susceptibility of a limited proportion of people at a given age to gastrointestinal cancer and an associated tendency of some carcinogens including those in cigarettes and coal to promote malignancy in the intestines; thus, more intestinal cancers and fewer gastric cancers are seen in countries where the environmental content of those carcinogens is high.

270. ARTIFICIAL SWEETENERS AND HUMAN BLADDER CANCER.

Howe GR, Burch JD, Miller AB, Morrison B, Gordon P, Weldon L, Chambers LW, Fodor G, Winsor GM
Epidemiology Unit, Natl. Cancer Inst. Canada, Univ. Toronto, Ontario, Canada
Lancet; 2(8038):578-581 1977

A study on the correlation between the use of artificial sweeteners and bladder cancer was conducted based on the results of questionnaires obtained from 480 men and 152 women with bladder cancer. The risk ratio for men who had used the sweeteners vs those who had never used them was 1.6; there was a significant dose-response relationship for both the duration and frequency of use. Joint controlling for both smoking and instant coffee consumption were used so that the relationship between these variables and artificial sweetener consumption was independent. It was not possible to determine the composition of each artificial sweetener used since the composition of saccharin and/or cyclamate had changed over the years; however, 82% of the men reported the use of saccharin only. Male diabetics who did not use sweeteners were at a decreased risk, but those who did use them had the same risk as the nondiabetic men. For women, there was a nonsignificant decreased use of artificial sweeteners among the cancer cases. (15 Refs)

271. COFFEE DRINKING AND CANCER OF THE LOWER URINARY TRACT.

Simon D, Yen S, Cole P
Harvard Sch. Public Health, Boston, Mass.
J Natl Cancer Inst; 54(3):587-591 1975

Coffee drinking habits of urban white women from Massachusetts and Rhode Island were studied for a possible relationship to lower urinary tract (LUT) cancer. Patients with LUT cancer were chosen from the pathology log book and diagnostic index of participating hospitals. Three white women were chosen as controls for each case. Data on coffee drinking and related habits were obtained by mail questionnare for 135 women with LUT cancer and for 390 controls; questions included age when coffee drinking and cigarette smoking began, usual daily consumption of coffee, cigarettes, and tea, occupation, coffee additives used, and type and strength of coffee. The risk ratio for women who drank one or more cups of coffee per day was 2.1 when compared to women who drank no coffee or less than one cup per day. However, the amount of coffee consumed showed no relationship to dose-response. The type of coffee, the strength of the coffee or the use of creamers or sugar substitutes (i.e saccharin or cyclamates) was not associated with increased risk of disease. The risk of LUT cancer for cigarette smokers as compared to nonsmokers was 1.6. The results suggest that the association of coffee drinking with LUT cancer is noncausal.

272. COFFEE DRINKING AND CANCER OF THE LOWER URINARY TRACT.

Cole P
Harvard Sch. Pub. Hlth., Boston, Mass.
Lancet; 1(7713):1335-1337 1971

Interviews were conducted with 468 patients in the Boston area who had cancer of the renal pelvis, ureter, bladder or urethra; results confirmed the association of bladder cancer risk with cigarette smoking. In addition, an association was found between coffee drinking and bladder cancer risk. When data were controlled for age, cigarette smoking and occupation it was found that the numbers of observed and expected cases of bladder cancer among drinkers of less than 1 cup of coffee per day were 29 vs. 41.3, resp, among males and 9 vs. 22.9, resp, among females. Among drinkers of more than 4 cups of coffee per day, the numbers of observed and expected bladder cancer cases were 84 vs. 71.8, resp, among males and 22 vs. 19.4, resp, among females. Data yielded relative risks of developing bladder cancer of 1.24 for male coffee drinkers and 2.58 for female coffee drinkers; the risk of developing bladder cancer for persons who drank no coffee was 1.00. The association of bladder cancer and coffee drinking was stronger for women than for men; among male coffee drinkers the cancer risk increased with age.

273. A RETROSPECTIVE STUDY OF RENAL CANCER WITH SPECIAL REFERENCE TO COFFEE AND ANIMAL PROTEIN CONSUMPTION.

Armstrong B, Garrod A, Doll R
Radcliffe Infirmary, Oxford OX2 6HE, Great Britain
Br J Cancer ; 33(2):127-136 1976

The authors interviewed 106 patients with adenocarcinoma of the renal parenchyma, 33 patients with carcinoma of the renal pelvis, and 139 individually matched control patients. Comparison of the cancer patients with the control patients showed no evidence of a positive association between either type of renal cancer and coffee or animal protein consumption. However, a statistically significant negative association between cheese consumption and cancer of the renal pelvis suggested that animal protein may protect against this type of cancer by increasing the metabolic rate of carcinogens.

274. EFFECT OF SMOKING ON CAFFEINE CLEARANCE.

Parsons WD, Neims AH
Dept. Pharmacology and Therapeutics, McGill Univ., McIntyre Medical Sciences Building, 3655 Drummond St., Montreal, Quebec H3G 1Y6, Canada
Clin Pharmacol Ther; 24(1):40-45 1978

The elimination of caffeine from saliva was compared in groups of healthy smokers (13) and nonsmokers (13). Mean caffeine half-life in smokers (3.5 hr) was shorter than that in the nonsmokers (6.0 hr). The body clearance of caffeine in the smokers (155 +/-16 ml/kg/hr) was greater than that in the nonsmokers (94 +/-18 ml/kg/hr) (p less than 0.05). No significant difference was noted in the apparent volume of distribution in smokers (720 +/-67 ml/kg) and nonsmokers (610 +/-80 ml/kg). These differences probably reflect the induction of hepatic aryl hydrocarbon hydroxylase activity in smokers. The increased clearance of caffeine by smokers may contribute to the higher consumption of coffee reported to occur in this group. (Author abstract) (33 Refs)

VI. OTHER NON-RESPIRATORY TRACT CANCERS ASSOCIATED WITH TOBACCO PRODUCTS

EDITOR'S NOTE: Section VII lists comparative epidemiological studies dealing with multiple cancer sites.

275. EPIDEMIOLOGY OF LIVER CANCER.

Arima M
Natl. Cancer Inst. Hosp., Tokyo
Jpn J Clin Med; 26(8):1833-1838 1968

Primary liver tumors were seen in 2076/106,992 patients autopsied in Japan from 1958-1965 (inclusive); the incidence was about 1.7-2.2% of all autopsies/yr. The ratio of hepatomas to cholangiomas was 8:1; the male:female ratios in patients with these tumors were 6:1 and 2:1, resp. Cirrhosis, usually of the Laennec type, was seen in about 63% of the males and 58% of the females with hepatoma; the incidence of cirrhosis was lower in patients with cholangioma (especially in females). Ridit analysis suggested an increased relative risk of hepatoma (with or without cirrhosis) in persons eating meat or drinking alcoholic beverages every day. Analysis of data for 180 patients with primary liver tumors indicated an over-all relative risk of about 4.5 in heavy smokers (over 30 cigarettes/day) and a somewhat lower relative risk (below 4.0) in ex-smokers. Positive family histories, obtained from 343 patients with hepatoma (212 with and 131 without cirrhosis) and 37 with cholangioma, included family histories of liver cancer (with or without cirrhosis) in 9.9%, 4.6% and 5.4%, resp, other liver diseases in 10.8%, 9.2% and 5.4%, resp, and cancer of other organs in 22.6%, 20.6% and 24.3%, resp. Autopsy examination of the livers of 46 patients previously treated with Thorotrast (radioactive 232ThO2) showed cholangioma in 19/46 (79.2%), hepatoma and hemangioendothelioma in 5/46 each (20.8%) and liver cirrhosis in 13/46 (38.4%). The mean survival times after Thorotrast inj in these 4 groups were 23, 28, 28 and 21 yr, resp.

276. RETROSPECTIVE STUDY ON NASOPHARYNGEAL CARCINOMA.

Lin TM, Chen KP, Lin CC, Hsu MM, Tu SM, Chiang TC, Jung PF, Hirayama T
Natl. Taiwan U. Coll Med., Taipei
J Natl Cancer Inst; 51(5):1402-1408 1973

Nasopharyngeal carcinoma (NPC) was identified among 442 residents of Northern and Southern Taiwan over a 1.5 yr period. Interviews were conducted with 343 of these patients and 1017 nondiseased residents of the same areas. The average annual incidence rate for NPC was 4.2/100,000 population: 5.8 for males; 2.4 for females; 4.5 for Northern Taiwan; 3.8 for Southern Taiwan; 3.2 for the Taiwanese; and 9.9 for the Mainlanders. The age-specific incidence rates rapidly increased in the 30-to-34-yr-old age group, continued to increase gradually until they reached a peak in the 55-59 age group, and declined in the older age groups. Smoking was significantly associated with NPC in that persons smoking more than 20 cigarettes/day stood twice the risk of developing NPC as those who never smoked. Working under poorly ventilated conditions also doubled the risk of NPC. In addition, some basal symptoms and the use of herb drugs and nasal balms or oils were associated with a higher risk of NPC. The data indicate that the etiology of NPC is probably multifactorial.

277. DESCRIPTIVE AND ANALYTICAL EPIDEMIOLOGY OF NASOPHARYNGEAL CANCER.

Hirayama T
Epidemiology Div., Natl Cancer Center Res. Inst., Tsukiji-5, Chuo-ku, Tokyo, Japan
IARC Sci Publ; 20:167-189 1978

Data on the descriptive and analytical epidemiology of nasopharyngeal carcinoma (NPC) that have been reported since the first international symposium on the subject in Singapore in 1964 are reviewed. NPC is rare in most countries in the world, with an age-adjusted incidence rate of less than 1/100,000, and the incidence rate is twice as high in men as in women. The southern Chinese have a uniquely high risk, the incidence rates per 100,000 being 10-20 in men and 5-10 in women. The greater the admixture of southern Chinese blood in a given ethnic group, the more likely it is that the NPC incidence rate in that group will be raised. The incidence in both sexes begins to rise after the ages of 20-24 and reaches a plateau at between 45 and 54. When the logarithm of mortality and morbidity is plotted against the logarithm of age the power of the age that provides the best fit to a straight line on a log-log graph is approx two to four. These figures are lower than those for other cancer. Seroepidemiological case-control studies indicate that both different birthplace and abnormal response to Epstein-Barr virus (EBV) antigen significantly enhance the risk for NPC; when these two factors are combined, the relative risk appears to rise further. The effect of other environmental chemicals, ie, those in cigarette smoke, shown to be significant in several retrospective studies, could explain in part epidemiological phenomena such as sex difference in incidence. The definitive reason for the uniquely high risk in southern Chinese should be further investigated by taking into account the interactions of host factors (birthplace, histocompatibility antigens, etc) and environmental factors (Epstein-Barr virus, chemical carcinogens including nitrosamines, excessive intake of salted fish, nutritional deficiencies, etc). (103 Refs)

278. EPIDEMIOLOGY OF MALIGNANT TUMOURS OF THE NASOPHARYNX IN FRANCE: RETROSPECTIVE AND PROSPECTIVE STUDIES.

Brugere J, Point D, Sancho-Garnier H, Schwaab G
Head and Neck Unit, Medical Section, Fondation Curie, Paris, France
IARC Sci Publ; 20:241-249 1978

The results of a retrospective and a prospective epidemiological study of French patients with malignant tumors of the nasopharynx are presented. Among 641 adults with malignant tumors of the nasopharynx treated at two French centers between 1951 and 1976, 80% had nasopharyngeal carcinomas (NPC), and 16% had malignant lymphoma. Malignant lymphomas, embryonal sarcomas, and epidermoid carcinomas were the only malignancies observed in 54 children treated at one center between 1952 and 1973. Among the total 509 NPC patients, the male:female ratio was 3:1. Most cases were observed between the ages of 40 and 59 yr. Only 38% percent of the patients treated at the Institut Gustave Roussy and 59% of those seen at the Fondation Curie were French. A prospective study led to the collection of data on 133 new malignant nasopharyngeal tumor patients treated between 1975 and 1976. Of these patients, only 54 were French. Most well-differentiated carcinomas (79%) occurred in Western Europeans. The male:female ratios for lymphoepitheliomas, undifferentiated carcinomas, and malignant lymphomas were 2:1, 3:1, and 1:1, respectively, but the ratio for well-differentiated carcinoma was 20:1. Patients with epidermoid carcinomas smoked twice as much as patients with lymphoepitheliomas. (1 Ref)

279. DISCUSSION OF RISK FACTORS FOR NASOPHARYNGEAL CARCINOMA.

Henderson BE, Louie E

Dept. Community and Family Medicine, Univ. Southern California Sch. Medicine, Los Angeles, CA

IARC Sci Publ; 20:251-260 1978

Seven case-control studies of nasopharyngeal carcinoma (NPC) in southern Chinese populations, conducted from 1961-1974, are reviewed. 'Never married' and lower socioeconomic statuses were risk factors in most studies. A prior history of ear and nose disease and of the use of traditional Chinese medication (balms or oils) for nasal symptoms was a relatively consistent finding. Chinese tea was associated with NPC in some studies, but not in others. Alcohol consumption and smoking were not regularly associated with NPC risk. Most of the studies found an increased risk associated with exposure to inhaled smoke, fumes, and/or dust. For US subjects, contact with such carcinogens would occur primarily at the workplace, whereas, for the Chinese, exposure would occur primarily in the home during childhood. The high risk for NPC in southern Chinese may also be due to exposure to Cantonese salted fish, in which carcinogenic nitrosamines have been detected. One study found a positive association between exposure to salted fish during the weaning period and NPC risk. Experimental carcinoma of the nasal cavity was induced in rats fed a diet of Cantonese salted fish or exposed to N-nitrosodimethylamine by artificial inhalation. Further study of the dietary patterns of the southern Chinese, especially during childhood, are needed. (28 Refs)

280. ENVIRONMENTAL FACTORS IN THE ETIOLOGY OF NASOPHARYNGEAL CARCINOMA: REPORT ON A CASE-CONTROL STUDY IN HONG KONG.

Geser A, Charnay N, Day NE, De-The G, Ho HC

International Agency Res. Cancer, Lyon, France

IARC Sci Publ; 20:213-229 1978

Environmental factors that may contribute to the development of nasopharyngeal carcinoma (NPC) were investigated in a casecontrol study of 150 NPC patients, hospital controls, normal controls, and healthy controls living in the same households as the NPC patients. Significantly more NPC patients belonged to the four lowest occupational classes than controls p less than 0.01, relative risk (RR) 3.17. More NPC patients than controls adhered to Buddhism and ancestor worship (p less than 0.01, RR 2.1) and had a history of ear or nose illness after the age of 15 yr (p less than 0.001). Consumption of bread and tinned food and the use of fennel, mustard paste, chili sauce, and Chinese wine as spices or flavorings were significantly less frequent in the patients than in controls. NPC patients also consumed green tea less frequently than controls (p less than 0.05, RR 0.57). There was a higher proportion of cigarette smokers among male controls than among NPC patients. Seventy-five percent of the mothers of NPC patients said that they had fed their babies salted fish after weaning, compared with 53.4% of the control mothers (p less than 0.01, RR 2.6). Multivariate analysis showed that traditional life-style and the consumption of salted fish during weaning are independent risk factors for NPC. (12 Refs)

281. CARCINOMA OF THE MAXILLARY ANTRUM AND ITS RELATIONSHIP TO TRACE METAL CONTENT OF SNUFF.

Baumslag N, Keen P, Petering HG

Div. Preventive Medicine, Dept. Environmental Health, Univ. Cincinnati Coll. Medicine, Cincinnati, OH, 05219

Arch Environ Health; 23(1):1-5 1971

Social habits and customs are related to different disease patterns. Snuff inserted in the nares has been shown to be associated with the incidence of antral carcinoma in the Bantu. Carcinoma of the maxillary antrum constitutes 45.5% of all the respiratory tract cancers in the Bantu. A pilot study was conducted to examine the trace metal content in samples of Swazi snuff by atomic absorption spectrometry. The metals analyzed were zinc, chromium, copper, lead, nickel, and cadmium. Samples of soot from Swazi huts were also analyzed for the same metals. The Swazi snuff showed high concentrations of nickel, chromium, and zinc. Since nickel and chromium in some forms are known carcinogens, the association between carcinoma of the maxillary antrum and snuff may be prevented if the source of trace metal contamination is eliminated. (Author abstract) (30 Refs)

282. EFFECT OF SMOKING DURING PREGNANCY ON THE RISK OF CANCER IN CHILDREN.

Neutel CI, Buck C

Dept. Comm. Med. U. Western Ontario, London, Canada

J Natl Cancer Inst; 47(1):59-63 1971

Smoking histories were ascertained for mothers of 89,302 infants and the incidence of cancer in these infants was determined to establish whether prenatal smoking is related to cancer in offspring. Among children of mothers who smoked 1 package of cigarettes or less/day (including nonsmokers) the incidence of cancer was 13.8 cases/100,000 child yr, package of cigarettes or more/day the cancer incidence was 10.7 cases/100,000 child yr. This differences was found not to be statistically significant. The relative risk of cancer development for children of light and heavy smokers combined, compared to the risk for nonsmokers was 1.3. It was concluded that, while in utero exposure to tobacco smoke probably does not have a carcinogenic effect on the fetus, a lesser general effect or an effect confined to a single tissue may be produced.

283. EPIDEMIOLOGY OF BRAIN TUMORS IN CHILDREN.

Gold EB

Johns Hopkins Univ., Baltimore, MD

Diss Abstr Int B; 39(2):665 1978

This study was primarily designed to follow-up leads from animal experiments by investigating the association of brain tumors in children with various hormonal factors and with a variety of chemical carcinogens. In the first phase of the study children with brain tumors diagnosed in the Baltimore area between 1960 and 1975 were identified from hospital records and death certificates. These records were abstracted and the data were used for the analysis of incidence, mortality and survivorship. The second phase of the study consisted of a case-control study designed to elucidate possible factors that might be associated with the development of brain tumors in children. In this phase, interviews were conducted with the parents of cases whose tumors were diagnosed between 1965 and 1975 and with the parents of two types of controls. The first control group, called the normal group, consisted of children selected from birth certificate files and matched to cases on date of birth (within 1 yr), race and sex. The second control group consisted of children with malignancies other than brain tumors who were matched to cases by race, age at diagnosis, date of diagnosis, and sex. Analysis of the data yielded several interesting findings. First, some support was given to the possibility that hormonal factors might be associated with brain tumors in children. Males, both white and black, in general had higher incidence rates than females, though males had poorer survival rates than females. In addition, the only age group in which males did not have higher incidence rates was at about the age of puberty. Also, mothers of cases tended to reach menarche at a younger or older age than mothers of controls. No differences were observed with respect to maternal use of oral contraceptives. More households of cases than of controls were exterminated for insects, and more mothers of cases than controls continued smoking during pregnancy, indicating an association between chemical carcinogenesis and brain tumors. Furthermore, more mothers of cases than of controls took barbiturates during pregnancy. No differences were observed in occupational chemical exposures of the parents. Possible etiologic involvement of oncogenic animal viruses was suggested by the increased exposure of cases to farm animals and sick household pets. (no Refs)

284. NICOTINE AND COTININE IN BREAST FLUID.

Hill P, Wynder EL
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Cancer Lett; 6(4):251-254 1979

Breast fluid aspirated from the nipples of 13 healthy, menstruating women (5 smokers and 8 nonsmokers) was assayed for nicotine and its major metabolite cotinine. With the smokers, a blood sample was taken and breast fluid aspirated 30 min after smoking. Neither nicotine nor cotinine could be detected in the plasma or breast fluid of nonsmokers, but in smokers both were detected in the breast fluid 30 min after smoking. The similarity of the nicotine levels in the breast fluid and plasma suggests that nicotine passes rapidly into the fluid but cotinine passes less readily. Further analysis of the breast fluid in various female populations may provide leads as to whether components are present that may be related to breast carcinogenesis. Breast fluid may contain many or all factors that contribute to the induction of breast cancer. (9 Refs)

285. CANCER OF THE PROSTATE AMONG MEN WITH BENIGN PROSTATIC HYPERPLASIA.

Greenwald P, Kirmss V, Polan AK, Dick VS
New York State Dept. Hlth., Cancer Control Bur., Albany
J Natl Cancer Inst; 53(2):335-340 1974

The occurrence of prostate cancer, the cause of death, and the epidemiologic features of prostatic hyperplasia were studied among 838 patients who had had subtotal prostatectomies for benign prostatic hyperplasia and 802 age-matched controls. All subjects were less than 80 yr old, the average age being 63 yr. Patients were followed for 10.7 yr and controls for 11.2 yr. Prostate cancer developed among 24 of the patients and 26 of the controls. This difference was not significant, the estimated relative risk of developing prostate cancer being 0.88 for both groups. Using the modified life-table method, the prostate hyperplasia patients were followed for 8115 person-yr, while the controls were followed for 8290 person-yr. Among the former group, there was no significant correlation between the development of prostate cancer and the weight of the hyperplastic gland originally removed. The incidence of bladder cancer did not differ between patients and controls. The patients and controls did not differ significantly in terms of marital status, race, occupation, or place of birth or death. Coffee was used slightly, but not significantly, more frequently by the patients than by the controls; the two groups did not differ in terms of diabetes, drug-use history, family medical history, or smoking or drinking habits. It is concluded that statistical analysis for interactions between prostatic hyperplasia and prostatic cancer revealed no association between the two diseases.

286. GENITAL HERPESVIRUS IN THE ETIOLOGY OF HUMAN CERVIX UTERI CANCER. (PP. 211-229)

Kessler II
Dept. Epidemiology, Johns Hopkins Univ., Baltimore, MD, 21205
Prevention and Detection of Cancer. Part I. Prevention. Vol. 1. Etiology. Proceedings of the Third International Symposium on Dectection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 1193 pp., 1977.

Two investigations of the possible role of herpesivuruses in cervical cancer (CC) were made. The first was a retrospective, case-control study of 350 Yugoslavian women with histologically confirmed squamous carcinoma of the uterine cervix and 350 matched controls. Herpes simplex virus type 2 (HSV-2) antibody titers were higher among the CC patients than the controls. The relative risk of CC in women positive for HSV-2 was significantly increased, even after adjustments were made for the effects of 34 epidemiologic factors associated with CC. In addition, compared with controls, women who developed CC were more likely to smoke and drink alcoholic beverages, they had higher blood pressures, their parents tended to be older at their birth, they had more multiple marriages and an earlier start of sexual activity, consistently reduced coital frequency, and they were more likely to have normal menstrual histories. There was an unexpected two- to threefold greater mortality, especially at younger ages, of the first husbands of the CC patients, compared with the control first husbands. In a second study, still in progress, two large groups of women are being observed: one married to men who, at some other time, had wives who developed CC and a second married to men without such histories. To date, abnormal pap tests have been found in 13.6% of the "case" wives vs 7.2% of the control wives. CC or carcinoma in situ has been diagnosed in 3.5% of the case wives and 1.2% of the control wives. These data support an etiological role for HSV-2 in CC and they suggest that hormonal factors may also be involved. (23 Refs)

287. LOW NATURAL KILLER-CELL ACTIVITY AND IMMUNOGLOBULIN LEVELS ASSOCIATED WITH SMOKING IN HUMAN SUBJECTS.

Ferson F, Edwards A, Lind A, Milton GW, Hersey P
Kanematsu Memorial Inst., Sydney Hosp., Sydney, N. S. W., Australia
Int J Cancer; 23(5):603-609 1979

A study was conducted to determine whether an association between smoking and the increased incidence of cancer may be due to an effect on natural killer (NK) activity. Age- and sex-matched normal smokers (60) and nonsmokers (59) and male smoking (13) and nonsmoking (27) melanoma patients were studied with respect to the NK activity of their WBC against cultured melanoma and Chang cells. In addition, serum IgG, IgM, and IgA levels and erythrocyte (E) rosette levels were assessed in the normal subjects. The WBC NK activity of the normal subjects and melanoma patients who were smokers against cultured melanoma target cells was much lower than that of the nonsmokers. The same trend was seen against the Chang target cells, but it was not as pronounced. Smokers had lower IgG and IgA, but not IgM, levels in their sera than nonsmokers. There was no significant difference in the percentage of T cells, measured as E rosettes, between the nonsmoking and smoking groups. The changes in NK activity and Ig levels may explain the link between smoking and the increased incidence of malignancy. These results suggest that a closer examination of the effects of smoking on the immune system in relation to malignancy is warranted. (33 Refs)

288. INDIVIDUAL DIFFERENCES IN MUTAGENIC SENSITIVITY IN HUMAN LYMPHOCYTES (MEETING ABSTRACT).

Falek A, Madden JJ, Shafer DA
Georgia Mental Health Inst., Emory Univ., Atlanta, GA
Am J Hum Genet; 30(6):118A 1978

Our studies of unscheduled DNA synthesis (UDS), sister chromatid exchange (SCE) and chromosome damage (CD) in human lymphocytes have shown that individuals consistently differ in their cellular genetic response to different drugs and environmental agents. The lymphocytes were first stressed with such mutagens as far UV (254 nanometers) or mitomycin C and then measured for induction of UDS (excision repair), SCE and CD. All individuals (n greater than 100) in this program were questioned as to their use of drugs, tobacco, alcohol and coffee. Also included in the program were a number of opiate addicts (n greater than 25) and methadone maintenance patients (n greater than 25). While the measure values for UDS, SCE and CD were found to be reliable for a given individual, great diversity of response was found for the population as a whole. Several environmental factors, particularly opiate addiction and smoking tobacco, were found to affect one or more of our assays significantly, but use of methadone, alcohol or coffee did not produce such differences. Since the environmental factors we investigated did not account for the observed wide range of response, we were therefore left with the possibility that either there were unknown environmental factor(s) affecting our measurements or, more likely, that these phenomena are genetically controlled. In either case, these measurable variations are important in terms of environmental pollution and human carcinogenesis because they indicate that a significant proportion of the population is more predisposed to serious genetic damage than would have previously been expected. (no Refs)

289. EFFECT OF SMOKING ON THE RECURRENCE OF MALIGNANT MELANOMA.

Shaw HM, Milton GW, McCarthy WH, Farago GA, Dilworth P
Melanoma Clinic, Sydney Hosp., Macquarie St., Sydney, New South Wales 2000, Australia
Med J Aust; 1(6):208-209 1979

The influence of smoking on the recurrence of malignant melanoma (MM) was studied in 1,908 Australian MM patients. At the time of diagnosis, 45.3% of the men and 28.1% of the women patients were smokers. Sites of primary lesions were similar in smokers and nonsmokers, but significantly more smokers than nonsmokers were less than 50 yr of age (p less than 0.01 for men; p less than 0.001 for women). There was a nonsignificant tendency for more smokers than nonsmokers to have regional lymph node or distant metastases at first presentation. Among the men with Stage I MM diagnosis, the proportion of patients who were diease-free 5 yr later was significantly lower (p less than 0.02) among smokers than nonsmokers (55% of 315 vs 63.0% of 403). A similar effect was not observed in the women patients. (8 Refs)

VII. COMPARATIVE EPIDEMIOLOGY OF TOBACCO-RELATED CANCERS (MULTIPLE SITES)

290. CANCER STATISTICS, 1974 - WORLDWIDE EPIDEMIOLOGY.

Silverberg E, Holleb AI
Am. Cancer Soc., New York, N. Y.
CA; 24(1):2-21 1974

Epidemiologic data are presented for cancer of the following sites: stomach, colon, rectum, lung, breast, uterine cervix, prostate and bladder. Data are also presented for leukemia. Stomach cancer mortality rates are high in Chile, Japan, Austria, Iceland, Central Europe, Finland, and U.S.S.R, but low in the U.S, Australia, New Zealand, Canada, and Israel. A diet rich in starches and low in fresh fruits and vegetables seems to be related etiologically. Mortality rates from colon and rectal cancer are high in North America, Australia, New Zealand, and Eastern Europe, but low in Central America and the Caribbean, Sub-Saharan Africa, the Eastern Mediterranean, Southwest Asia and Japan. There is an increased risk of colon and rectal cancer in patients with a history of ulcerative colitis, diverticulitis, appendicitis, polyps, or familial polyposis. Again, diet had been implicated etiologically. Lung cancer rates are high wherever death-registration systems are used and low in most of Africa and Asia. Multiple factor relationships have been observed in cigarette smokers exposed also to either asbestos or radon. Death rates from breast cancer are high in many countries, but low in the U.S.S.R, Japan, parts of the Far East, Africa and the Caribbean. The identifiable risk groups are indicated. Morality rates for cancer of the uterine cervix are high in Latin America and in parts of Africa and Asia, but are low in Europe, North America, Australia and New Zealand. Cervical cancer is related to sexual activity and is uncommon in communities where cleanliness is stressed. Prostatic cancer rates are high in Canada, the U.S, France, Belgium, Netherlands, Switzerland, Scandinavia, Australia, and New Zealand, but low in most of Asia, Africa, and Latin America. Some relationship may exist between endocrine function and prostatic cancer. Mortality rates from bladder cancer are high in parts of South America, England, Scotland, and the U.S; death rates are low in Asia, several Caribbean countries, Ireland, Norway, and Sweden. Persons at risk include cigarette smokers, patients with a history of chronic bladder infection or kidney stones, and aniline dye workers. Leukemia death rates show slight variations throughout the world, but they are usually higher in Jews than in Catholics or Protestants. Leukemia can be caused by excessive exposure to radiation; its relationship to viruses remains unclear. Estimates of cancer incidence are based on rates derived from the National Cancer Institute's Third National Cancer Survey.

291. COMPARATIVE EPIDEMIOLOGY OF CANCERS OF THE UNITED STATES AND JAPAN.

Wynder EL, Hirayama T
Div. Epidemiology, American Health Foundation. 1370 Ave. of the Americas, New York, NY 10019
Prev Med; 6(4):567-594 1977

A comparative epidemiological survey of the US white population and the general Japanese populations was made to determine whether differences in cancer incidence are related to specific environmental differences. Although malignant neoplasms are the second leading cause of death in the US and Japan, there is a wide variance in rates for particular sites. A major difference is seen for cancer of the prostate, colon, buccal cavity, skin, lungs, and urinary bladder and leukemia, for which US men display higher death rates. Japanese men and women exhibit higher mortality rates for cancer of the stomach, esophagus, and liver. US women have greater mortality from breast and uterine cancer. In both countries, death rates for cancer of the trachea, bronchus, and lung are increasing. Death rates for cancer of the prostate, bladder, and intestine are increasing in Japan and decreasing in the US. Japanese rates are approaching those for US whites. The consumption of cigarettes and dietary fats is sharply increasing in Japan. Environmental factors and dietary and social habits play an important role in the development of chronic diseases. (70 Refs)

292. GEOGRAPHIC DISTRIBUTION OF HEAD AND NECK CANCERS IN THE UNITED STATES. (PP. 40-44)

Fraumeni JF
C307 Landow Bldg., 7910 Woodmont Ave., Bethesda, MD 20014
Head and Neck Cancer. State of the Art Conference. February 16, 17 and 18, 1976. Vol. 88, St. Louis, MO, Larynogoscope, No. 1, Part 2, Suppl. 8, 1978.

The total number of cancer deaths between 1950 and 1969 and age-adjusted rates according to sex and race were determined for all US counties (except those in Alaska and Hawaii), and the incidence of various cancers was plotted on maps. Tumors of the nasal cavity and sinuses show some clustering in men in Texas and Louisiana. Rates of this cancer are significantly higher among men and women in counties with high concentrations of chemical industries. Among men, cancer of the oropharynx occurs excessively in the urban northeast and is consistent with tobacco and alcohol consumption. For women, this cancer predominates in the southeast, and it is associated with the po use of snuff. Salivary gland cancer is clustered in men in the Florida panhandle, Alabama, Mississippi, and Louisiana. However, a separate analysis has shown that the highest rates occur in Alaskan Eskimos. Nasopharyngeal cancer in men shows clustering in Maryland and the coastal areas of North Carolina. People in areas with high concentrations of chemical industries and high rates of nasopharyngeal carcinoma are also prone to bladder cancer. Esophageal cancer is clustered in the northeast in men and the southeast in women. Laryngeal cancer is common in the northeast, particularly around New York City, and along the southeast Atlantic coast and Gulf Coast. There is a high mortality for thyroid cancer in the north central area and the Rocky Mountain states.

293. GEOGRAPHIC PATTERNS OF CANCER MORTALITY IN THE UNITED STATES. (PP. 343-359)

Hoover R, Mason TJ, McKay FW, Fraumeni JF
Persons at High Risk of Cancer, an Approach to Cancer Etiology and Control. Fraumeni Jr. JF, ed. New York, Academic Press, Inc, 554 pp., 1975.

Twenty years of cancer mortality data (1950-1969) for the 3,056 individual counties in the contiguous United States are being used to derive geographic patterns of cancer mortality. The data have been analyzed on the basis of urban-rural and social class ratios. In both sexes a large urban effect was observed for cancers of the nasopharynx, larynx, colon, and rectum. Positive social class and urbanization effects were seen for breast cancer and Hodgkin's disease for women, but the urbanization effect for colon cancer disappeared when social class differences were controlled. The data also suggest that the excess mortality from cancer of the uterine cervix among white women in the southeastern United States can be attributed to the predominance of this cancer in the rural lower socioeconomic classes. When melanoma mortality rates for eight zones of latitude, standardized for age, urbanization, and social class differences were compared, there was a trend of increasing mortality from North to South. Following the same procedure, there was a gradient of declining mortality from North to South for Hodgkin's disease in white women. When Pearson product-moment correlation coefficients were calculated among cancer sites for white men and women in all 3,056 counties, cancers of the lung, larynx, and mouth and throat were highly correlated among men (smoking complex), as were cancers of the colon, rectum, esophagus, and bladder (urban complex). Among white women, cancers of the colon, rectum, breast, and ovary were all highly correlated and probably reflect both urbanization and social class determinants. In counties where the chemical industry is highly concentrated, excessive mortality from cancers of the bladder, lung, liver, and certain other sites was found. The major contribution of the county resource will probably be to identify geographic clusters suggesting etiologic clues, which can then be pursued by analytic studies.

294. GEOGRAPHIC CLUES TO HIGH-RISK GROUPS IN CANCER.

Fraumeni JF
Environmental Epidemiology Branch, NCI, NIH, Bethesda, MD, 20014
Cancer Bull; 29(6):191-194 1977

The mapping of cancer mortality by county and then correlating the data with demographic and environmental data allow the formulation of hypotheses for the causes of cancer. These maps indicate that in men and women, the death rates for all cancers are highest in the northeastern section of the country and in southern Louisiana. Colon cancer mortality is highest in the northeast and lowest in the south. There is also a high death rate in rural farming communities in southeastern Nebraska. Persons who migrate from low-risk to high-risk areas and vice versa take on the risk feature of the area to which they migrate. Deaths from stomach cancer are clustered in the north-central and southwestern areas of the country for whites and in southern Louisiana for blacks. The highest rates for lung cancer are found along the Gulf of Mexico and along the southeastern Atlantic coast. Rates are also high in the northeast and around metropolitan areas. Counties with paper, chemical, petroleum, shipbuilding, and nonferrous smelting industries had the highest mortality. Bladder cancer mortality for men is high in New Jersey, in urban areas along the Great Lakes, and in rural New York and New England; for women, the rates are highest in northern New England. Breast cancer parallels the distribution of colon cancer. Oropharyngeal cancer in men is highest in the urban northeast, consistent with patterns of tobacco smoking and alcohol consumption, but oral cancer in women is highest in the south. Snuff is a suspected etiological agent in the latter area. Rates for esophageal cancer parallel those for oral cancer. (18 Refs)

295. CANCER BY COUNTY: ETIOLOGIC IMPLICATIONS. (PP. 21-32)

Blot WJ, Mason TJ, Hoover R, Fraumeni JF
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20014
Incidence of Cancer in Humans, Proceedings of the Cold Spring Harbor Conferences on Cell Proliferation. Vol. 4, Hiatt HH, Watson JD, Winsten JA, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Origins of Human Cancer., 602 pp., 1977.

Lung, colon, and oral and pharyngeal cancer incidence was determined in various counties throughout the US, and the results were correlated with those of analytical field studies. In white men, lung cancer mortality was elevated in the Northeast and around large metropolitan areas, but the highest rates were clustered in contiguous counties along the Gulf of Mexico and the Southeast Atlantic coast. Rates among women were high in urban areas. In general, rates were lowest in farming areas; mortality was inversely correlated with county education levels. Mortality among white men was elevated in counties with paper, chemical, and petroleum manufacturing industries. Geographic patterns for colon cancer mortality were identical for men and women. For both sexes and among races, high rates were present throughout the Northeast and low rates were present throughout the South. High mortality rates were associated with urbanization, income, and ethnicity (Irish, German, Czechoslovakian). Colon cancer did not appear to be associated with dietary habits. High mortality from oral cancer among white men predominated in the Northeast, while high rates in white women were clustered in the Southeast. The northern excess among men was attributed to urbanization, tobacco smoking, and alcohol consumption. It is suspected that the po use of snuff among southern women accounts for their excess of oral cancer. Among men, oral cancer mortality was elevated in counties with leather industries, particularly in the central US. Other findings include high skin cancer rates in the South, high bladder cancer rates in men in industrial areas, high stomach cancer rates in Northern European and Spanish American ethnic groups, and rectal cancer rates paralleling those of colon cancer. Studies of cancer mortality in counties grouped according to specific environmental variables are reviewed. (31 Refs)

296. ASSOCIATION OF CANCER SITES WITH TOBACCO AND ALCOHOL CONSUMPTION AND SOCIOECONOMIC STATUS OF PATIENTS: INTERVIEW STUDY FROM THE THIRD NATIONAL CANCER SURVEY.

Williams RR, Horm JW
Dept. Internal Medicine, Univ. Utah Coll. Medicine, Salt Lake City, UT 84121
J Natl Cancer Inst; 58(3):525-547 1977

From personal interviews with 7,518 invasive cancer patients obtained in the Third National Cancer Survey, the quantitative lifetime use of cigarettes, cigars, pipes, unsmoked tobacco, wine, beer, hard liquor, and combined alcohol were recorded, as well as education and family income level. In an initial screening analysis of these data, Mantel-Haenszel 2 x 2 contingency tabulations and multiple regression analyses were used to compare each specific cancer site with controls from other sites to test for associations with exposure variables. Significant positive associations with cigarette smoking were found for cancers of the lung, larynx, oral cavity, esophagus, stomach, pancreas, bladder, kidney, and uterine cervix. Other forms of tobacco were associated with cancers of the oral cavity, larynx, lung, and cervix. Consumption of wine, beer, hard liquor, and all combined showed positive association with neoplasms of the oral cavity, larynx, esophagus, colon, rectum, breast, and thyroid gland. College education and high income showed positive associations with cancers of the breast, thyroid gland, uterine corpus, and melanomas in men. These indicators of high socioeconomic status showed inverse associations with invasive neoplasms of the uterine cervix, lung, lip-tongue, and colon in women. College attendance (but not income) showed an inverse association with stomach cancer and positive association with pancreatic cancer in men. Still other tumor sites showed "suggestive" associations with each of these exposure variables. In this study, age, race, sex, smoking, drinking, education, income, parity, foreign birth, marital status, and geographic location were used as stratification variables separately or in combination, to assess and control their potentially confounding affects and to examine between exposure and control variables within a stratum. (41 Refs)

297. VITAL STATISTICS OF THE UNITED STATES. 1960. (PP. 427)

Anon
Dept Health, Education and Welfare Public Health Serv
Vital Stat US; 2(pt A): 1963

Mortality from neoplasms in the U.S is treated in section 1, "Mortality Analysis and Summary". In 1960, death rates (per 100,000) for neoplasms was second in rank for white males, white females and nonwhite males (166.1, 139.8 and 134.1, resp); it was third for nonwhite females (109.8). It is treated in more detail in section 5, "General Mortality Tables". Four tables deal with deaths from 255 selected causes: these deal with analysis by month; by specified race and sex; by age, race, and sex; and by color and sex (U.S and each state). Deaths and death rates for 59 selected causes are also dealt with by age, color, and sex.

298. A SEQUENTIAL SPACE-TIME CLUSTER ANALYSIS OF CANCER MORTALITY IN THE UNITED STATES: ETIOLOGIC IMPLICATIONS.

Burbank F
Natl. Cancer Inst., Bethesda, Md.
Am J Epidemiol; 95(5):393-417 1972

A cluster analysis and a time-trend analysis were performed on cancer mortality figures for the United States from 1950-1967. For males, 33 tumor types fitted into one of five geographic clusters and 15 tumor types remained unclustered. For females, 34 tumor types were clustered and 16 unclustered. Time-trend analysis showed rising and falling incidences of tumor types (reticulum cell sarcoma was found to be the most rapidly rising tumor type). When cancer mortality in each of the five cluster areas was divided into rising and falling categories, it became possible to postulate 11 hypothetical carcinogens associated with the 33 clustering tumor types in men and women. One hypothetical carcinogen was postulated to be the causal agent for reticulum cell sarcoma, lung, hypopharynx, floor of mouth, pancreas and six other cancers with a rising incidence. These cancers clustered in the New England and Great Lakes regions. The carcinogen was postulated to be related to cigarette smoking. Solar radiation and "endocrine factors" were two other actual carcinogenic agents which were provisionally identified among the hypothetical carcinogens. Each hypothetical carcinogen was the cause of more than two diverse tumor types, and each had determined the predominant geographic and temporal distribution of the tumor types with which it was associated.

299. COMPARATIVE EPIDEMIOLOGY OF TOBACCO-RELATED CANCERS.

Wynder EL, Stellman SD
Div. Epidemiology, Naylor Dana Inst. Disease Prevention, American Health Foundation, New York, NY 10019
Cancer Res; 37(12):4608-4622 1977

In a retrospective study, interviews eliciting information on smoking habits were obtained from 3,716 patients with cancer of the lung (Kreyberg types I and II), mouth, larynx, esophagus, or bladder and greater than 18,000 controls. For each of these cancers, the relative risk of smokers of both sexes increased with the quantity smoked and the duration of the habit. The strongest increase occurred for cancer of the lung and larynx, the least increase for cancer of the esophagus and bladder. For ex-smokers, the risk decreased with years of cessation. The risk for mouth cancer of pipe and cigar smokers, who inhaled much less than cigarette smokers, was less than that of the latter and increased with the quantity smoked. The risk of mouth, larynx, and esophagus cancer among smokers increased with the quantity of alcohol consumed. Greater smoking habits and lesser cessation rates were noted among lower socioeconomic groups, suggesting that these groups will develop an ever-increasing proportion of tobacco-related cancers. (43 Refs)

300. LONGEVITY, SELECTIVE MORTALITY, AND COMPETITIVE RISKS IN RELATION TO CHEMICAL CARCINOGENESIS.

Hammond EC, Garfinkel L, Lew EA
Dept. Epidemiology and Statistics, American Cancer Society, 777 Third Ave., New York, NY, 10017
Environ Res; 16(1/3):153-173 1978

Male cigarette smokers and nonsmokers were compared periodically with respect to longevity, total death rates, deaths from cancer (all sites combined), and deaths from cancer of three specific sites: lung, pancreas, and bladder. The data were obtained through questionnaire surveys of men in 22 states, the starting date for the analyses being July 1, 1960, and the ending dates June 30, 1975, for men born in 1887 or earlier and June 30, 1971, for men born later than 1887. The findings were compared with the results calculated for three hypothetical types of cigarettes: LCA, which induce the same lung cancer rates as ordinary cigarettes but have no other effects; BPCA, which increase death rates from bladder and pancreatic cancer; and CA, which yield the same age-specific death rates from cancer of every site and type as ordinary cigarettes. Life expectancy at age 40 was 37.85 yr for nonsmokers, 34.87 yr for light smokers, and 30.79 yr for heavy smokers. The proportion of men living to age 65 was 86.04% for nonsmokers, 79.61% for light smokers, and 70.55% for heavy smokers. The proportions of men living to age 85 were 29.12%, 20.15%, and 9.7%, respectively, for the three groups. The mean ages at death from cancer were 74.93 for nonsmokers, 73.66 for light smokers, and 70.83 for heavy smokers. CA smokers had the same age-specific cancer death rates as ordinary cigarette smokers; LCA smokers, the same age-specific lung cancer death rates as ordinary smokers; BPCA smokers, the same bladder and pancreas death rates as ordinary smokers. Otherwise, the death rates in these three groups were the same as those for nonsmokers. (no Refs)

301. EFFECT OF CIGARETTE SMOKING ON CONNECTICUT RESIDENTS.

Christine BW, Sullivan PD
Conn. St. Hlth. Dept.
Conn Health Bull; 85(1):23-28 1971

The incidence of malignant diseases associated with cigarette smoking in Connecticut was investigated. Heart disease and cancer, the leading causes of death in the state as in the nation, have accounted for increasing numbers of deaths in recent yr. The rate of deaths from heart disease in 1925 in Connecticut was 179.1 deaths/100,000 population and 336.6/100,000 in 1969. Cancer of the respiratory system in Connecticut had an incidence of 14 cases/100,000 in 1935 among males and 70 cases/100,000 in 1970; among Connecticut females, the increased incidence has not been marked, with the incidence/100,000 cases being 5 in 1935 among 9 in 1970. Cancer (all sites) accounted for 272 deaths among Connecticut residents in the 25-44 yr age group in 1969 and 1,843 and 2,894 deaths in the 45-64 yr and 65 yr age groups, resp. Cancer of the larynx has shown a steadily increasing percentage of cases in males (66.4% in 1965 and 71.9% in 1966). Males in Connecticut have also showed increasing rates for cancer of the esophagus and bladder, which are 2 other sites of cancer thought to be causally related to cigarette smoking.

302. LOW CANCER INCIDENCE AND MORTALITY IN UTAH.

Lyon JL, Gardner JW, Klauber MR, Smart CR
Dept. Family and Community Medicine, Div.
Epidemiology, Univ. Utah Coll. Medicine, 50 North Medical Drive, Salt Lake City, UT 84132
Cancer; 39(6):2608-2618 1977

Utah cancer mortality for the yr 1950-1969 and morbidity for the yr 1966-1970 are reported. Utah had 18% fewer cases of cancer than expected based on the Third National Cancer Survey, and 24% fewer cancer deaths than expected based on national mortality data. Cancer sites associated with cigarette smoking and alcohol use accounted for nearly half of these differences. Several major sites not strongly associated with smoking showed lower incidence and mortality than expected. These included pancreas, colon, rectum, female breast, uterine cervix and ovary. A marked excess occurrence above expectation was observed for cancer of the lip. Some possible explanations of these findings are discussed, including some of the unique aspects of the Utah population. (Author abstract) (47 Refs)

303. CANCER MORTALITY AMONG MORMONS.

Enstrom JE
Sch. Public Health, Univ. California, Los Angeles, Calif. 90024
Cancer; 36(3):825-841 1975

A study was conducted on cancer mortality among Mormons (a religious group) in which the use of tobacco, alcohol, coffee, and tea is forbidden and the use of wholesome grains and fruits and moderations in meat consumption are recommended. Initial indications are that Mormons as a whole smoke and drink about half as much as the general population, and that active Mormons abstain almost completely from tobacco and alcohol. They appear to be similar to the general white population in other respects such as socioeconomic status and urbanization. Data were taken from state mortality figures, from church records, and from a 1965 Alameda County, California study of health and life-styles. Preliminary results show that the 1970-1972 cancer mortality rate among California Mormon adults is about one-half to three-fourths that of the general California population for most cancer sites, including many sites with an unclear etiology. The average age-adjusted total mortality ratio for nonsmokers at least 35 yr old to United States white men in 1960 was 55%, with a range from 46-64% in the eight studies from which these figures were taken. The 1970-1972 age-adjusted total mortality ratio for California Mormon men at least 35 yr old was 46-69%, depending on the age distribution assumed. These mortality rates may considerably overestimate the mortality rates for observant lifetime Mormons, because a large proportion of Mormons have followed or still follow a life-style similar to the general population: 40% of Mormons in California are converts, having entered the church as adults, and another 40% are inactive and tend to ignore Mormon health practices. Low cancer rates as those seen in the Mormons have not been observed in any other group of Americans except Seventh-day Adventists. These low rates suggest the development and exploration of new etiologic hypotheses for cancer and may lead to understanding a lifestyle that produces low risk to cancer of all types.

304. SYNCHRONOUS AND METACHRONOUS SQUAMOUS CELL CARCINOMAS OF THE HEAD, NECK, AND ESOPHAGUS.

Thompson WM, Oddson TA, Kelvin F, Daffner R, Postlethwait RW, Rice RP
Dept. Radiology, Duke Univ. Medical Center, Durham, NC, 27710
Gastrointest Radiol; 3(2):123-127 1978

In a series of 3,287 patients with squamous carcinoma of the head and neck and 640 patients with esophageal carcinoma, there were 35 patients with separate primary tumors of the head-neck and esophagus (34 men, 1 woman); 34 had the diagnosis of the head-neck tumor established either before or at the same time as the esophageal cancer. Double primary tumors occurred synchronously in 9/34 patients. In 1 patient, carcinoma of the esophagus was diagnosed 1 yr before squamous cell carcinoma of the head and neck. Twenty-six patients had an interval of greater than 6 mo between the diagnosis of the two tumors. Approx 1% of the patients studied had synchronous or metachronous head and neck and esophageal tumors. Primary tumors of the head and neck were diagnosed by direct endoscopy; those with carcinomas of the esophagus had the diagnosis suggested by barium esophagogram. Seven of the patients with head and neck tumors were treated only with irradiation, while the remaining 28 patients had a combination of surgery and irradiation for the head and neck tumors. Complications included cervical esophageal stricture and mild dysphagia in the four patients with laryngeal tumors and mild swallowing dysfunction and dysphagia in the majority of patients who underwent extensive surgical procedures for head and neck tumors. One patient developed carcinoma of the esophagus in the radiation field 10 yr after exposure, while the remainder developed carcinomas at sites away from the radiation portals. The majority of patients had a history of heavy smoking and alcohol consumption. The need for strict, periodic, lifelong screening via barium esophagogram is emphasized because of increased incidence of esophageal carcinoma in those with squamous cell carcinoma of the head and neck. (15 Refs)

305. ASBESTOS AND SMOKING (LETTER TO EDITOR).

Selikoff IJ, Hammond EC

Mount Sinai Sch. Medicine, City Univ. New York, New York, NY

JAMA; 242(5):458-459 1979

The association between smoking, asbestos, and cancer is reviewed. The two most common asbestos-induced cancers are lung cancer and mesothelioma. The former is usually related to cigarette smoking, whereas the latter is not. Similarily, cancers of the esophagus, larynx, and oropharynx occur in excess primarily in asbestos workers who have a history of cigarette smoking, whereas the incidences of colorectal and renal cancers are increased in such workers regardless of smoking history. While asbestos by itself somewhat increases the risk of cancer, smoking by itself causes a major increase. One in every five deaths among asbestos workers is due to lung cancer. Smoking, which causes bronchitis, emphysema, and fibrosis, adds an undesirable and sometimes insupportable burden to asbestos-induced pneumoconiosis. All workers known to have been exposed to asbestos should be advised never to smoke or to stop smoking as soon as possible. Periodic medical surveillance would further reduce the risk of gastrointestinal, oropharyngeal, laryngeal, and renal cancers, and therapy for superimposed pulmonary infections would limit the incidence of asbestosis. (4 Refs)

306. CANCER MORTALITY AMONG LOW-RISK POPULATIONS.

Enstrom JE

Cancer Epidemiology, UCLA Sch. Public Health, UCLA, Los Angeles, CA

UCLA Cancer Cent Bull; 6(3):3-7 1979

The cancer mortality experience among the major low-risk populations in the US is reviewed. Over an 8-yr period, the mortality rates for cancer sites related to cigarette smoking or alcohol consumption were extremely low among a group of 47,000 Seventh-Day Adventists living in California. In addition, the risk of death from cancers of the colon, stomach, and pancreas was about 60%-70% that of the general US population, and for women the risk of postmenopausal deaths from cancers of the breast, ovary, and uterus was significantly below that of the general population; dietary factors were suggested as possible reasons for these findings. Compared with US whites, the cancer mortality ratio among Mormons during 1968-1975 was 66% for men and 81% for women. The total cancer death rate among active Mormon men greater than 35 yr old living in California is approx 50% that of US white men. The remaining life expectancy for these Mormons is 44.6 yr, 8 yr longer than that of US white men in 1970. The cancer death rates among Mormons were lower than those expected for all sites except the prostate and except for lymphomas and leukemias. Cancer mortality rates among US nonsmokers were 58%-76% lower than those for US whites. The most plausible explanation is that the lack of smoking per se reduces the total cancer rate by a substantial amount. Other factors that appear likely to have the greatest impact on cancer mortality are personal health habits, diet, socioeconomic status, and certain host factors related to aging. (10 Refs)

307. INTERRELATIONS OF TOBACCO, ALCOHOL AND DIET IN CONTRIBUTING TO CANCER INCIDENCE AMONG FIVE ETHNIC GROUPS IN HAWAII (MEETING ABSTRACT).

Hinds MW, Kolonei LN, Nomura AM

Epidemiology Program, Cancer Center of Hawaii, Univ. Hawaii, Honolulu, HI, 96822

Proc Am Assoc Cancer Res; 20:182 1979

From 1975 through 1977, we conducted a survey on a cluster sample of the population of Hawaii to determine the level of consumption of tobacco, alcohol and selected dietary items by persons age 18 and older. Over 20,000 persons were interviewed who belong to the ethnic groups of Japanese, Chinese, Filipino, Caucasian and Hawaiian/part-Hawaiian. Using multiple discriminate function analysis, we determined which dietary items best discriminated among the 10 ethnic-sex groups in terms of frequency of consumption. Age-adjusted incidence rates for cancer of the tongue, mouth, pharynx, larynx, esophagus, pancreas, colon and rectum experienced by the 10 ethnic-sex groups were determined by using the population-based Hawaii Tumor Registry. We then plotted the age-adjusted rates of consumption of the discriminating dietary items, tobacco and various forms of alcohol against the age-adjusted incidence rates. Consumption rates of tobacco, beer, wine, hard liquor and certain dietary items were found to be significantly correlated with cancer incidence rates for several sites. (no Refs)

308. PROSPECTIVE STUDIES ON CANCER EPIDEMIOLOGY BASED ON CENSUS POPULATION IN JAPAN (MEETING ABSTRACT). (PP. 15-16)

Hirayama T

Epidemiology Division National Cancer Center Research Institute, Tokyo, Japan

Third International Symposium On Detection And Prevention Of Cancer. 1976.

A population prospective study on the health consequences of selected risk factors including cigarette smoking and alcohol drinking has been in progress in Japan since the fall of 1965. 265,118 adults aged 40 years and above, 91-99% of the census population in the study area in 29 Health Center Districts in Japan, have been followed by establishing a record linkage system between the risk factor records, a current residence list obtained by specially planned annual census, and death certificates. A total of 24,668 deaths, including 6,484 cancer, occurred during the 9 year period. Age specific death rates for each cause of death in the study population were similar to those for the whole country. Both men and women who smoked cigarettes experienced significantly higher mortality ratio from cancer of all sites: m 1.67 (act 3043/exp 1819.4) f 1.35(410/302.9), cancer of lung: m 3.75(444/118.4) f 1.83(34/18.5), cancer of stomach: m 1.54(1332/862.7) f 1.34(137/102.1), cancer of liver: m 1.67(332/198.4) f 1.65(56/33.8). Cancer of esophagus and pancreas also showed higher mortality ratio in daily cigarette smokers in men: 2.61(172/65.9) and 1.50(127/84.3) respectively. Expected frequencies were calculated by applying age specific mortality rate for nonsmokers to daily smokers' population by age groups. A clear-cut dose-response relationship was demonstrated for the number of cigarettes smoked and the age at initiation of smoking. Similar analysis has been done with regard to other risk factors such as habit of alcohol drinking, of eating, occupation, residence, marital status, number of children etc. Multifactor-multidisease risk matrix has been constructed based on their materials and cancer high-risk and low-risk groups were identified. (Author Abstract)

309. A POPULATION PROSPECTIVE STUDY ON CANCER EPIDEMIOLOGY IN JAPAN (MEETING ABSTRACT). (P. 271)

Hirayama T

Epidemiology Natl. Cancer Center Res. Inst., Tokyo, Japan

Proceedings of the Japanese Cancer Association. The 36th Annual Meeting Held at Tokyo, Japan, October 1977. Japanese Cancer Association, Tokyo, Japan, 1977.

Two hundred sixty-five thousand, one-hundred eighteen adults, aged 40 yr and above, 95% of the census population in 29 health center districts, were interviewed in the fall of 1965. A record linkage system between the risk factor records, a current residence list and death certificates was established. Out of 2,419,844 person-yr of observation, 27,993, including 7,377 cancers, died by the end of 1975. Cancer high risk and low risk groups have been identified by multiple cross tabulation and matched group analysis. Cigarette smoking was identified to promote risks of cancer of all sites: mouth and pharynx, esophagus, stomach, liver, larynx, lung and cervix. Higher risk of cancer of the esophagus was found in daily alcohol drinkers and cancer of the pancreas, liver and breast in daily meat intakers. Lower risk of stomach cancer was observed in drinking two glasses of milk daily and lung and prostatic cancer in daily intakers of green and yellow vegetables. The risk-lowering effect of daily intake of green and yellow vegetables was noted in both sexes, in each age group, in each prefecture, and in both smokers and non-smokers.

310. CANCER EPIDEMIOLOGY IN JAPAN (MEETING ABSTRACT).

Hirayama T

Dept. Epidemiology, Natl. Cancer Center Res. Inst., Japan

J Jpn Soc Cancer Ther; 12:2 1975

High-risk cancer groups were epidemiologically studied. There was a clear-cut decline in the age adjusted death rate for stomach and uterine cervical cancer and a striking increase in lung and pancreatic cancer. The death rate from cancer of all sites will probably become 15% to 20% lower after 10 yr, especially in the middle age group. Cancers of the stomach, esophagus and liver are more frequent in Japan than in the Western countries; this is most probably due to the influence of diet. Stomach cancer was most prevalent in Tohoku and Hokuriki Districts facing the Japan Sea and least frequent in Okinawa. In Okinawa the incidence of stomach cancer was quite similar to that in Japanese in Hawaii. Breast cancer, which was also least frequent in Okinawa, however, was more frequent in Japanese in Hawaii. The results of a prospective study of 265,118 cancer patients (adults aged 40 and above) showed that both men and women who smoked daily experienced the highest death rate from cancer of all sites. A significantly higher risk in daily cigarette smokers was observed for cancers of the mouth, hypopharynx, esophagus, stomach, liver, pancreas, larynx, and lung in men and for cancers of the stomach, colon, liver, larynx, lung, cervix and bladder in women. A clear-cut dose-response relationship was observed in terms of number of cigarettes smoked and also of age at the start of smoking. A combined effect of smoking and daily meat intake and a combined effect of smoking and drinking were observed on cancer of the pancreas and on cancer of the esophagus, respectively. The nationwide registry of childhood leukemia showed a combined effect of genetic load (family history of leukemia and consanguinity marriage) and prenatal radiation on the risk of the disease. HB antigen carrier showed a high risk for hepatoma, and carrier of a high titer of antibody against Epstein-Barr virus demonstrated a high risk for cancer of the nasopharynx. Breast cancer was noted to be at high risk in women with early menarche, later marriage, later pregnancy and fewer children. The identification and management of cancer high risk groups is considered the basis of primary, secondary and tertiary cancer prevention. (no refs)

311. PROSPECTIVE STUDIES ON CANCER EPIDEMIOLOGY BASED ON CENSUS POPULATION IN JAPAN. (PP. 1139-1148)

Hirayama T

Epidemiology Div., Natl. Cancer Center Res. Inst., Tokyo, Japan

Third International Symposium on the Detection and Prevention of Cancer held by the International Study Group for the Prevention and Detection of Cancer in New York, April 26-May 1, 1976. Part I, International Study Group for the Prevention and Detection of Cancer New York, NY, Vol. 1, 1193 pp., 1977.

The 9-yr follow-up results of a Japanese prospective study on the health consequences of cigarette smoking and alcohol consumption are presented. Among the 265,118 adults (aged greater than or equal to 40 yr) studied, there was a total of 24,668 deaths, 6,485 from cancer. Men and women who smoked cigarettes daily had the highest death rates from cancer, and the risk was particularly high when smoking was initiated during adolescence. Smoking significantly increased the risk of cancer of all sites, the risk of cancer of the mouth, pharynx, esophagus, stomach, liver, pancreas, larynx, and lungs in men, and the risk of cancer of the mouth, stomach, liver, larynx, and lungs in women. Daily alcohol consumption enhanced the risk of cancer of the mouth, pharynx, esophagus, liver, and lungs in men and cancer of the esophagus and lungs in women. The risk among occasional drinkers was nearly identical to that of nondrinkers. Among individuals who were both smokers and drinkers, there was an elevated risk for digestive tract cancers, including cancer of the mouth, pharynx, esophagus, and liver. The risk of laryngeal and lung cancer was enhanced by smoking, regardless of drinking habits, but the risk of digestive tract cancers were selectively high when smoking and drinking were combined. Thus, the oncogenicity of cigarette smoking in the larynx and lung differs from that in the digestive tract. It is suggested that the former represents contact carcinogenesis and the latter metabolic carcinogenesis. (3 Refs)

312. MORTALITY IN RELATION TO SMOKING: 20 YEARS' OBSERVATIONS ON MALE BRITISH DOCTORS.

Doll R, Peto R

Dept. Regius Professor Medicine, Radcliffe Infirmary, Oxford OX2 6HE, England

Br Med J; 2(6050):1525-1536 1976

In 1951 the British Medical Association forwarded to all British doctors a questionnaire about their smoking habits, and 34,440 men replied. With few exceptions, all men who replied in 1951 have been followed for 20 yr. The certified causes of all 10,072 deaths and subsequent changes in smoking habits were recorded. The ratio of the death rate among cigarette smokers to that among lifelong non-smokers of comparable age was, for men under 70 yr, about 2:1, while for men over 70 yr it was about 1.5:1. These ratios suggest that between a half and a third of all cigarette smokers will die because of their smoking, if the excess death rates are actually caused by smoking. To investigate whether this is the case, the relation of many different causes of death to age and tobacco consumption was examined, as were the effects of giving up smoking. Smoking caused death chiefly by heart disease among middle-aged men (and, with a less extreme relative risk, among old men), lung cancer, chronic obstructive lung disease, and various vascular diseases. The distinctive features of this study were the completeness of follow-up, the accuracy of death certification, and the fact that the study population as a whole reduced its cigarette consumption substantially during the period of observation. As a result lung cancer grew relatively less common as the study progressed, but other cancers did not, thus illustrating in an unusual way the causal nature of the association between smoking and lung cancer. (Author abstract) (49 Refs)

313. A COHORT ANALYSIS OF U.K. CANCER INCIDENCE TRENDS FOR CERTAIN SITES (MEETING ABSTRACT). (PP. 180-190)

Waterhouse JA
Birmingham Regional Cancer Registry, Birmingham, England
Proc Int Cancer Congr 11th. Vol. 3 (Cancer Epidemiology, Environmental Factors). Florence, Italy, October 20-26, 1974. Bucalossi P, Veronesi U, Cascinelli N, ed., New York, American Elsevier, 1975.

Evidence for 1960-1971 trends in morbidity rates of cancer of certain anatomical sites was assessed on the basis of statistics accumulated at the Cancer Registries of Birmingham in the British midlands and of the southeastern part of England including half of the London area. Mean annual incidence rates by site, sex and age for three time periods in a span of 12 yr were computed and the points plotted to form a cohort incidence line. In their composite pattern, the cohort incidence lines closely approximated the contour incidence curves which represented the morbidity risk by age for a given time period. Similar to the trend world-wide, the rate of incidence of stomach cancer declined in younger age groups. The rate of incidence of cancer of the breast in females and ovarian cancer increased in younger populations, whereas in older females the rate of endometrial cancer has increased. Rates for cancer of the bladder, pancreas, larynx and bronchus all showed definite increases. Among males, the rate of increase of lung and laryngeal cancer has diminished to zero; however, in females it has been increasing sharply. Evidence incriminating cigarette smoking in lung and laryngeal cancer is very strong. Morbidity data from cancer registries may provide information of predictive value.

314. SEX DIFFERENCES IN THE INCIDENCE OF TUMOURS AT VARIOUS SITES.

Ashley DJ
Morriston Hosp., Swansea, Wales
Br J Cancer; 23(1):26-30 1969

Data from 3 sources (5 continents; England + Wales 1958-1963; 10 U.S metropolitan areas) were used to study the age-adjusted frequencies of 34 cancers (excluding cancers of the reproductive organs) in males and females. The female:male ration (5 continents) for all tumors was 0.88:1. With the exceptions of malignant melanoma, thyroid cancer and cancer of the colon, the tumors listed were more prevalent in males than in females. The cyclic hormonal activity of the female might affect the incidence of thyroid cancer (the 5-continent female:male ratio was 2.33:1, compared to 16.5:1 in the U.S non-white group) and malignant melanoma (5-continent female:male ratio of 1.20:1). The discrepancy seen between cancer of the colon and cancer of the rectum (5-continent female:male ratios of 1.04:1 and 0.67:1, resp) was not explained. The male preponderance for lung, lip, larynx and bladder cancer was attributed to environmental factors (smoking, occupational carcinogen exposure). Except for cancer of the reproductive organs, the data suggested that females have 40-70% the chance of developing cancer as males. The possibility that females might have a greater immunologic potential because of the presence of the paired X chromosome (which carries at least 1 gene concerned with immunoglobulin production) is discussed.

315. ALCOHOL CONSUMPTION, CIGARETTE SMOKING, CANCER AND RELATED DISEASES IN WESTERN SCOTLAND (MEETING ABSTRACT).

Gillis CR, Hole DJ, Boyle P
Cancer Intelligence Unit, Ruchill Hosp., Glasgow, Scotland
Br J Cancer; 40(2):301-302 1979

The West of Scotland has traditionally been associated with a high incidence of lung cancer and a high frequency of alcoholism. A retrospective case-control study has been carried out on a single-blind basis among approx 2,000 hospital patients broadly representative of the general population of Western Scotland. This paper explores the relative and attributable risks for various cancers in relation to detailed history of cigarette smoking habits and alcohol consumption analyzed for both these factors separately and in combination. Each 'case' has been compared with 2 age- and sex-matched controls. Validity checks of the data have been instituted. The results are presented in relation to lung, colon, bladder and other cancers for which epidemiological associations have been established with either cigarette smoking, alcohol consumption or both. The results form part of an international collaborative study being carried out in France, Austria, Italy, Germany, the United States of America and Cuba, and the West of Scotland shows interesting differences. While some of these may simply be related to differences in incidence, the size of the observed differences between Scotland and the other countries strongly argues the implication of some other major factor amidst the groups being studied. At present, differences in nutritional status appear to be the most fruitful avenue for further exploration. (no Refs)

316. A CANADIAN STUDY OF SMOKING AND HEALTH - SECOND REPORT.

Best EW, Walker CB
Div. Epidemiol., Dept. Natl. Health Welfare, Ottawa, Ont., Canada
Can J Public Health; 55(1):1-11 1964

Results of a study were presented, mainly of 77,922 male pensioners (World Wars I, II and Korean War) but excluding those hospitalized, made between July 1956 and June 1962. Comparison of age-specific death rates for all causes of death combined show that for males age 30 and over, the excess observed deaths over the expected number for nonsmokers for all who smoked cigarettes only was 52%.

317. A CANADIAN STUDY OF SMOKING AND HEALTH.

Department of National Health and Welfare
Dept. Natl. Health and Welfare, Ottawa, Canada
A Canadian Study of Smoking and Health. Ottawa, Department of National Health and Welfare, Canada, 137 pp., 1978.

A long-term study was initiated in 1955 by the Canadian Department of National Health and Welfare with the cooperation of the Department of Veterans Affairs to investigate the relationships between residence, occupation, and smoking habits to the mortality from chronic diseases, particularly lung cancer. The study includes information on the characteristics of the response and nonresponse population, the overall effects of smoking on mortality in males, analysis of the effects of cigarette smoking-intensity, causes of death of nonsmokers and cigarette smokers, the effects of duration, inhalation, occupation, and residence, cigar and pipe smoking, and the effects of cigarette smoking on women. The study population consisted of Canadian war veteran pension recipients and their dependents. The outstanding finding of this study was that cigarette smokers had excessive mortality, especially from heart disease, lung cancer, bronchitis, and emphysema compared with nonsmokers.

318. TRENDS IN CANCER DEATH RATES IN THE LAST 50-60 YEARS, USING SWITZERLAND AS AN EXAMPLE.

Gsell O
U. Basel Gen. Hosp., Switzerland
Z Krebsforsch; 72(2):197-210 1969

Age-standardized death rates/10,000 living persons for all carcinomas combined, decreased by 10% in males and 25% in females in Switzerland from 1910-1960. Rates for stomach carcinoma decreased markedly, with smaller decreases in the rates for carcinoma of the esophagus and colon (both sexes), and a sharp decrease in carcinoma of the cervix (females), during this time. Rates for carcinoma of the bronchus increased in both sexes, especially in males (a 24-fold increase was seen in males); death rates for carcinoma of the pancreas remained approx stationary until 1940-1943, but doubled from that time to 1959-1962 (both sexes). The death rates for carcinoma of the prostate, ovary and female breast also increased. A comparison of these rates with the crude and standardized death rates for these and other tumors in 1952-1965, showed a continuance of the trends noted since 1910, except for decreased death rates for carcinoma of the ovary, breast and (after 1954) corpus uteri in females. In 1910, the 4 most frequent tumors seen in all age groups in males were GI carcinomas; after 1960, lung cancer was the most frequent tumor in males. A female preponderance was seen for gallbladder and thyroid cancer and a male preponderance (attributed to the effects of smoking) for cancer of the respiratory tract (mouth to bronchus) and bladder.

319. THE INTERACTIONS OF SMOKING, ENVIRONMENT AND HEREDITY AND THEIR IMPLICATIONS FOR DISEASE ETIOLOGY. A REPORT OF EPIDEMIOLOGICAL STUDIES ON THE SWEDISH TWIN REGISTRIES.

Cederlof R, Friberg L, Lundman T
Dept. Environmental Hygiene, Karolinska Inst., Stockholm, Sweden
Acta Med Scand Suppl; 612:105-128 1977

Using data compiled by the Swedish Twin Registries, the interactions of smoking, environment, and heredity on disease etiology were reviewed. Morbidity studies revealed associations between smoking and lung cancer and other respiratory diseases. (159 Refs)

320. TOBACCO SMOKING, OCCUPATION, AND MALIGNANT TUMORS IN THE RURAL POPULATION OF VRATSA, BULGARIA.

Nikolov I, Stoianov I, Stoichev I, Draganov I, Petkova-Bocharova T, Chernozemski I
Oncology Res. Center, Medical Acad., Sofia, Bulgaria
Onkologiia; 14(2):61-66 1977

Cancer incidence and its relationship to tobacco smoking and occupation were studied in 27 villages of the district of Vratsa, Bulgaria, during 1965-1974. Only subjects aged greater than 16 yr were considered. Tumors were found in 315/46,913 smokers and in 239/61,244 nonsmokers. The relative risk of tumors of the mouth, stomach, urinary bladder, and, especially, of the bronchi and lungs was significantly higher among smokers than nonsmokers (p less than 0.001), but there was no significant difference between these groups in the incidence of cancer of the renal pelvis, ureter and urinary tract. Compared with subjects of other occupations, farm workers were found to have increased risk of skin cancer (5.1x), cancer of the renal pelvis and ureter (3.3x), bladder cancer (3.3x), gastric cancer (2.1x), and labial cancer (2.1x). (18 Refs)

321. EPIDEMIOLOGICAL RESEARCH ON THE RELATIONSHIP BETWEEN TOBACCO, ALCOHOL AND CANCER.

Flamant R
Departement de Statistique Medicale de l'Institut Gustave Roussy, Villejuif, France
Prog Biochem Pharmacol; 14:36-46 1978

Epidemiologic studies of the relationship between tobacco, alcohol, and cancer are reviewed. Cancers associated with smoking are those of the lung, larynx, pharynx, oral cavity, esophagus, and bladder. All except esophageal cancer are related to the amount smoked, and lung, laryngeal, and bladder cancer are related only to the inhalation of cigarette smoke. Two studies show that the risk of lung cancer is reduced in men smoking filter-tipped cigarettes and in men who have quit smoking. Based on studies in different countries, it is hypothesized that the cancer risk varies with the kind of tobacco smoked. Alcoholism is associated with increased mortality from cancers of the esophagus, hypopharynx, and other sites in the upper respiratory and alimentary tracts. The effect of alcohol is limited to certain geographic areas and is less important than that of tobacco. Upper respiratory and alimentary cancers are related nearly equally to the use of tobacco and alcohol. To a certain extent, the higher the correlation between the sites and the use of tobacco and alcohol, the higher the male:female sex ratio. (10 Refs)

322. TOBACCO CRAVING.

Bernhard P
47 Kaiser Friedrich St., Duisburg-Hamborn 41, Germany
Med Monatsschr; 18(8):344-348 1964

The higher incidence and aggravation of various diseases in smokers (as compared to nonsmokers) are discussed and reviewed. Per 100 patients, incidence of cancer by site for smokers and nonsmokers, was, resp: larynx, bronchus, and oral mucosa, 90+% and less than 10%; pharynx, tongue, lips, and urinary tract, 80+% and less than 20%; esophagus, rectum and anus, 60+% and less than 40%; gastric cancer, about 50% and 50%. Skin and intestinal cancers were more frequent in nonsmokers. Tobacco craving is viewed as a serious social and health problem.

VIII. OBSERVATIONS ON THE EFFECTS OF MODIFIED TOBACCO PRODUCTS IN MAN

323. LESS HAZARDOUS CIGARETTES. (PP. 791-804)

Gori GB
Div. Cancer Cause and Prevention, NCI, Bethesda, MD
Prevention and Detection of Cancer. Part I. Prevention. Vol. 1. Etiology. Proceedings of the Third International Symposium on Dectection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 1193 pp., 1977.

A summary of the developments that have led to an acceptable, less hazardous cigarette is presented. Tobacco chemistry, culture, curing, blending and processing, epidemiological and other studies relevant to smokers, bioassay techniques for evaluating cigarettes, cigarette construction, and organoleptic characteristics of cigarettes are discussed. (64 Refs)

324. TOWARD LESS HAZARDOUS CIGARETTES.

Gori GB, Lynch CJ
Div. Cancer Cause and Prevention, NCI, Bethesda, MD, 20014
JAMA; 240(12):1255-1259 1978

Critical levels of selected cigarette smoke constituents have been expressed in terms of max numbers of pre-1960 cigarettes that a smoker may consume daily without increasing his mortality risk substantially above that of a nonsmoker. This could still imply an important risk, although it may be difficult to detect. We relate these levels to the yields of 27 current low tar and nicotine commercial cigarettes, as measured at the Oak Ridge National Laboratory. In addition, the yields of these selected constituents concomitant with the yield of 1 mg of nicotine are provided as a guide for the smoker who titrates or adjusts his smoking pattern to accommodate a fixed daily intake of nicotine. (Author abstract) (20 Refs)

325. LOW-RISK CIGARETTES: A PRESCRIPTION. LOW-TOXICITY CIGARETTES HOLD SIGNIFICANT PROMISE IN THE PREVENTION OF DISEASES RELATED TO SMOKING.

Gori GB
Div. Cancer Cause and Prevention, NCI, NIH, Bethesda, MD, 20014
Science; 194:1243-1246 1976

Antismoking education campaigns in our society have met with only partial success: today 55 to 60 million Americans smoke, and the habit is increasing among teenagers and women. It is important to protect individuals who continue to smoke despite all warnings. There is evidence that this can be accomplished in at least two ways. First, it may be possible to remove toxic smoke components and thus reduce specific hazards. Second, the dose-response evidence suggest that, if the total intake of smoke can be reduced, after an appropriate time a reduction in disease incidence should occur. The technology to achieve these results has been developed and can be applied to the manufacture of commercial cigarettes. These cigarettes will not conform to traditional flavor patterns, but consumer perception can be made to change and compensating flavors and fragrances can be added. The feasibility of less hazardous cigarettes raises the question of whether there are limits of cigarette and smoke composition that may approach relative safety. These limits can be defined as the smoke intake doses at which the risk of disease in smokers approaches that in nonsmokers. Such values can be estimated by dose-response analysis of several epidemiological studies and by extrapolation of blood concentrations at different rates of intake for certain smoke components, such as carbon monoxide. Critical values determined by these methods should not be interpreted as indicators of safe smoking levels; they do imply, however, that a rapid shift in cigarette consumption habits toward the proposed range of values will make possible a substantial reduction in the current epidemic proportions of smoking-related diseases. (Author abstract) (53 Refs)

326. "LOW-RISK" CIGARETTES: THE DEBATE CONTINUES (2 LETTERS TO EDITOR).

Gart JJ, Schneiderman MA, Gori GB
3406 Kenilworth Drive, Chevy Chase, MD, 20015
Science; 204(4394):688-692 1979

The statistical methodology used in two recent articles on "low-risk cigarettes" is criticized. Some of the methodologic errors made in the handling of data relating the relative risks of cancer of the lung and bronchus to the number of cigarettes smoked per day are detailed. In reply, the author of the original articles states that the articles presented a realistic procedure for gradually reducing the levels of hazard and addiction for smokers who persist in their habit despite its known health consequences. Although this would not eliminate the risk to the smoker, it has the potential of reducing the current epidemic of diseases associated with smoking. (6 Refs)

327. TOWARD LESS HAZARDOUS CIGARETTES (2 LETTERS TO EDITOR).

Warner KE, Gori GB, Lynch CJ
Univ. Michigan Sch. Public Health, Ann Arbor, MI
JAMA; 241(20):2143-2144 1979

In a recent article, critical levels of selected cigarette smoke constituents expressed in terms of pre-1960 cigarettes were translated into equivalent numbers of present-day low-tar and -nicotine cigarettes to help smokers wean themselves to less-hazardous cigarettes. The analysis in this article was based on some highly questionable assumptions that, if wrong, challenge the validity of the conclusions. Also, the article did not take into account relative risks of certain high-risk groups. Thus, the article did not provide any scientifically meaningful evidence that certain present-day smoking behaviors will result in statistically nondetectable health risks. In reply, the authors of the original article state the basis for their assumptions and evidence supporting them. The entire thrust of the article was to suggest a method for changing present-day smoking behaviors through progressively less hazardous and less addictive smoking stages. (2 Refs)

328. SOCIALLY TOLERABLE CIGARETTE SMOKE (2 LETTERS TO EDITOR).

Homburger F, Gori GB, Lynch CJ
Bio-Res. Inst., Cambridge, MA
JAMA; 241(20):2142-2143 1979

An article that gave the impression that some cigarettes are relatively safe to smoke in limited quantity is criticized. The number of current cigarettes that would expose the smoker to amounts of tar, nicotine, carbon monoxide, nitrogen oxides, hydrogen cyanide, and acrolein that were tolerated without demonstrable effect with pre-1960 cigarettes was calculated. However, such extrapolation from pre-1960 cigarette smoke to today's smoke would be justified only if the composition of the diluted smoke remained basically the same. The manipulations necessary to obtain lower yields of the six substances under consideration, alter the proportions of other ingredients and may change the biologic activity of the smoke. Only a valid and practical in vivo bioassay of the smoke itself, as it is inhaled by human smokers, can discriminate between hazardous and less-hazardous smoke. The authors of the original article replied that tests with greater than 130 types of experimental cigarettes confirm that todays cigarette processing reduces known toxic constituents quantitatively and that there is no evidence of an increase in other suspect toxic constituents. The authors agreed on the need for an in vivo bioassay of the smoke itself. (4 Refs)

329. SOME RECENT FINDINGS CONCERNING CIGARETTE SMOKING. (PP. 101-112)

Hammond EC, Garfinkel L, Seidman H, Lew EA
Dept. Epidemiology and Statistical Res., American Cancer Society, New York, NY, 10017
Incidence of Cancer in Humans, Proceedings of the Cold Spring Harbor Conferences on Cell Proliferation. Vol. 4, Hiatt HH, Watson JD, Winsten JA, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Origins of Human Cancer., 602 pp., 1977.

Some recent findings concerning the effects of cigarette smoking are discussed. Death rates are higher in smokers than in nonsmokers, and they increase with the number of cigarettes smoked per day and with the number of years spent smoking. A prospective study of greater than 1,000,000 subjects was carried out between 1959 and 1965, and the

897,825 subjects who were still alive in 1965 were studied until 1971 or 1972. For both men and women for both study periods, the adjusted number of deaths and the adjusted number of deaths from lung cancer were lowest among smokers of low tar and nicotine (T/N) cigarettes and highest among high T/N smokers. The adjusted number of lung cancer deaths was greater in subjects who smoked 20-39 low T/N cigarettes/day than in subjects who smoked 1-19 high T/N cigarettes/day. The overall death rate and the lung cancer death rate were far higher in subjects who smoked low T/N cigarettes than in subjects who never smoked regularly. Thus, reduction of the T/N content of cigarette smoke did not make cigarette smoking safe, although switching from high T/N to low T/N cigarettes would appear to be a small step in the right direction. (7 Refs)

330. BENEFITS OF STOPPING SMOKING. (PP. 777-779)

Garfinkel L
Dept. Epidemiology and Statistics, American Cancer Society, Inc., New York, NY
Prevention and Detection of Cancer. Part I. Prevention. Vol. 1. Etiology. Proceedings of the Third International Symposium on Dectection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 1193 pp., 1977.

The long-range benefits of stopping smoking are reviewed with particular reference to epidemiological studies that show the effects on the mortality rate and pathologic studies demonstrating the effects on human tissues. The damage to bronchial epithelium and coronary arteries undergo some repair and the risk of dying from lung cancer and coronary heart disease decrease in proportion to the length of time stopped. (no Refs)

331. A THEORETICAL APPROACH TO THE EVALUATION OF THE MORTALITY EFFECTS OF A "LOW TAR" CIGARETTE.

Herson J, Simpson C, Kennedy J, Kapoor S
Department of Community Health Practice and Cancer Research Center, College of Medicine, Howard University, Washington D.C. 20059, U.S.A.
J Chronic Dis; 29(12):747-758 1976

The two parameter Gompertz hazard function is shown to fit Hammond's 1960 American Cancer Society life tables which depict survivorship of men aged 25-100 yr for five levels of smoking frequency. Using data on tar levels of cigarettes on the market during the period 1960-65, various models are proposed to estimate the covariation of the Gompertz parameters by smoking frequency and tar content. For each model, estimated life expectancy and age specific death rates are presented for various smoking frequency-tar groups and the mortality consequences of a "low tar" and "low frequency" public health policy are discussed. Multiple regression analysis is used to summarize the mortality findings and to provide a quantitative assessment of the relative importance of tar content and smoking frequency in determining life expectancy and death rate. Evidence from the models favors a "low tar" policy over a "low frequency" policy but considerable benefits can be obtained from a combined policy. (Author Abstract)

332. RECENT CHANGES IN TOBACCO PRODUCTS AND THEIR ACCEPTANCE BY THE CONSUMER.

Weber KH
Harvestehuderweg 88, 2000 Hamburg 13, W Germany
Bull Inf CORESTA; (Special):15-30 1976

Health warnings against the use of tobacco have led to changes in smoking habits by the consumer and a gradual decrease in the exposure of smokers to condensates through alteration of cigarette composition. Changes in the make-up of cigarettes during the past 20 yr are reviewed. Changes in condensate and nicotine are reviewed, and methods used to achieve the reductions are outlined; these include processing of the tobacco leaf, changes in cigarette paper, and, most importantly, the comprehensive introduction of cellulose acetate cigarette filters, which selectively remove some vapor phase constituents, such as volatile phenols. The modern cigarettes have been accepted by smokers, who do not compensate for the lessened content of condensate and nicotine per cigarette either by smoking more cigarettes, by increasing the puff vol or frequency, or by discarding shorter butts. Statistics are presented on the decrease of smoke per smoker; changes in the content of both the particulate phase constituents and vapor phase constituents are presented. Condensate and nicotine, and therefore all chemicals corresponding to the particulate phase, have been successfully decreased by about 50%, despite increased per capita cigarette consumption. Residues from agricultural chemicals such as aldrin, dieldrin, endrin and heptachlorepoxide have been greatly reduced.

333. LESS HARMFUL WAYS OF SMOKING.

Wynder EL, Hoffmann D
Amer. Hlth. Fdn., New York, N.Y.
J Natl Cancer Inst; 48(6):1749-1758 1972

Data on the relationship of cancer and smoking are reviewed, and evidence that different smoking habits are associated with different cancer risks is presented. Although cigar and pipe smokers are at less risk of developing lung cancer than cigarette smokers, excessive pipe and cigar smoking enhances cancer risk. Furthermore, cigar and pipe smokers have a high risk for cancer of the upper alimentary tract. Harmful agents in tobacco smoke are of three types: tumor initiators (including polycyclic aromatic hydrocarbons), tumor accelerators (including 9-methyl-carbazole and 1-methylindole) and tumor promoters (including phenol). Smoke from high- nitrate tobacco, from terpene -free tobacco stems, and from cigarettes made of reconstituted tobacco sheets appears to be less carcinogenic than smoke from conventional cigarettes. Reducing the amount of smoke coming in contact with lung tissue also appears to reduce cancer risk. In one study it has been shown that filter cigarette smokers of at least ten years duration have lower risks of developing lung cancer than non-filter smokers. The diminished risk for lung cancer among pipe and cigar smokers compared to cigarette smokers is probably related to diminished depth of inhalation of tobacco smoke among pipe and cigar smokers. The importance of monitoring human smoking habits in the evaluation of smoking hazards is stressed.

334. EFFECT OF FILTER CIGARETTES ON THE RISK OF LUNG CANCER.

Bross ID
Natl Cancer Inst Monogr; 28:35-40 1968

Data were obtained for 974 white men with lung cancer seen at the Roswell Park Memorial Institute in 1960-1963 and a corresponding group of men without malignant disease. The relative risk (in multiples of the nonsmoker risk) of lung cancer was studied in 200 patients currently smoking non-filter cigarettes and 65 patients using filter cigarettes. In 21 patients who smoked regular cigarettes (including those smoking over 1 pack/day) for 30 yr or less (low exposure to cigarette smoke) the relative risk was about 3; in 5 low-exposure patients smoking filter cigarettes it was 1.4. In "medium-exposure" patients (under 1 pack/day for 30-50 yr), the relative risks with regular and filter cigarettes (76 and 26 patients, resp) were 5.6 and 3.9, resp. In the "high exposure" group (over 1 pack/day for 30 yr or more), the relative risks with regular and filter cigarettes (64 and 25 patients, resp) were 12.0 and 5.4, resp. The differences were significant in all groups. It is concluded that filter cigarettes reduce the lung cancer risk by about 40%, by comparison to non-filter cigarettes, although the risk is still about 4-fold higher than in nonsmokers.

335. SUGAR CONTENT OF THE TOBACCO AND PH OF THE SMOKE IN RELATION TO LUNG CANCER RISKS OF CIGARETTE SMOKING.

Elson LA, Betts TE
Inst. Cancer Res. Sutton, England
J Natl Cancer Inst; 48(6):1885-1890 1972

More than 150 brands of cigarettes from various countries were examined in a study of the relation between sugar content of cigarette tobacco and pH of smoke. Cigarettes made from flue-cured, high sugar tobacco produced a smoke of acid pH that became progressively more acid during smoking. Cigarettes made from air-cured, low sugar tobacco produced a less acid smoke that became progressively more alkaline during smoking. The lower incidence of lung cancer in smokers of air-cured tobacco cigarettes may relate to the fact that nicotine is more readily absorbed at alkaline than at acid pH. To obtain the same degree of "nicotine satisfaction" as in smoking low sugar cigarettes, the smoker of acid smoke cigarettes must inhale deeply at a time when the tar content of the smoke is highest. The smoking public is unlikely to accept air-cured, low sugar cigarettes, but flue-cured cigarettes could be made safer by raising the pH of the smoke through additives such as urea and guanidine salts.

IX. REVIEWS

336. SMOKING AND HEALTH: A REPORT OF THE SURGEON GENERAL.

US Department of Health Education and Welfare
Office Assistant Secretary Health, Public Health Service, U.S. Dept. Health, Education, and Welfare, Washington, DC
Smoking Health Report Surg Gen. 1164 pp., 1979.

This new surgeon General's Report on Smoking and Health is a compendium of new data confirming the conclusions of the original report published in 1964 and it reveals, with dramatic clarity, that cigarette smoking is even more dangerous than was supposed in 1964. It presents sobering information about women and smoking. Evidence suggests that mothers who smoke during pregnancy may create long-term, irreversible effects on their babies. The female mortality rate from lung cancer was three times higher in 1978 than in 1964, and women who have smoking characteristics similar to those of men experience similar overall mortality rates. Health risks to smokers exposed to certain occupational hazards are dramatically increased, and they include workers in the asbestos, rubber, coal, textile, uranium, and chemical industries. New evidence has accumulated with respect to relationships between tobacco use and cancer of the larynx, oral cavity, esophagus, urinary bladder, kidney, and pancreas. Cigarette smoking is causally related to lung cancer in men and women, and the risk of developing lung cancer increases with increasing dosages of smoking, as measured by number of cigarettes smoked per day, duration of smoking, age of initiation of smoking, degree of inhalation, tar and nicotine content of cigarettes smoked, and several other measurements. Prospective studies have shown that mortality rates from cancer of the oral cavity, larynx, pharynx, and esophagus are approx equal in users of cigars, pipes, and cigarettes. Although several factors appear to be involved in lip cancer development, pipe smoking alone or in combination with other forms of smoking is causally related to this cancer. Pipe and cigar tobacco condensates have a carcinogenic potential comparable to that of cigarette condensates. (15 Refs)

337. SMOKING AND HEALTH.

Richmond JB
Assistant Secretary for Health, Public Health Service, NIH, Bethesda, MD, 20014
Public Health Rep; 94(2) 1979

Remarks on the new report of the Surgeon General 15 yr after the original report note that there is overwhelming evidence associating tobacco smoking with disabling and fatal diseases. Dangers faced by pregnant women, women using oral contraceptives, and children and teenagers developing the smoking habit are particularly stressed. (no Refs)

338. TOBACCO AND HEALTH.

Holbrook JH
Dept. Internal Medicine, Div. General Internal Medicine, Univ. Utah, Salt Lake City, UT
CA; 27(6):344-353 1978

Several aspects of the effects of tobacco on health are reviewed. Tobacco smoke contains complete carcinogens, cocarcinogens (tumor initiators and promoters), and tumor accelerators. Most of the known are found in the tobacco tar. A substantial part of the carcinogenicity of tar is due to polynuclear aromatic hydrocarbons such as benzo(a)pyrene, N-nitrosamines, and beta-naphthylamine (a potent human bladder carcinogen). Cogent epidemiological data, coupled with experimental and pathological evidence, establish cigarette smoking as the most important cause of lung cancer, which in 1977 will account for more cancer deaths (approx 89,000) than any other site. The av male cigarette smoker's risk of developing lung cancer is 10 times greater than that of the nonsmoker. Lung cancer death rates for women are lower than those for men, but recently they have been rising more rapidly than the latter. The risk of developing lung cancer is directly related to total cigarette smoke exposure, duration of smoking, age at initiation, depth of inhalation, and cigarette tar and nicotine levels. Smoking of cigarettes, pipes, and cigars is a significant factor in the development of cancer of the oral cavity, pharynx, larynx, and esophagus. Combined exposure to alcohol and cigarettes is associated with high esophageal, oral, and pharyngeal cancer rates. Carcinoma of the pancreas and bladder is also more common in smokers than in nonsmokers. (68 Refs)

339. TOBACCO. (PP. 102-125)

Wynder EL, Mabuchi K, Hoffmann D
Cancer Epidemiology And Prevention Current Concepts. Schottenfeld D, ed. Springfield, Charles C Thomas, 1975.

All epidemiologic studies have consistently shown a relationship between smoking and lung cancer. The relationship is stronger for the Kreyberg Group I types (squamous and oat cell carcinoma) but is also seen for Kreyberg Group II types (adenocarcinoma and terminal bronchiolar carcinoma). Any cigar or pipe smoke that is readily inhalable has the same carcinogenic potential as cigarettes. In the U.S., lung cancer mortality is much higher for males, and this is thought to reflect a sexual difference in smoking habits. The effect of cessation of smoking on reduction of cancer risk has been noted, and appears to be dependent on the duration and number of cigarettes consumed prior to cessation. Tobacco smoking of any type constitutes an etiologic factor in oral, esophageal, laryngeal, bladder, renal, and pancreatic cancer. Some of these relationships are tenuous, but the available data definitely indicate a dose-response relationship between exposure and lung cancer risk, and a correlation between lung cancer rates and per capita cigarette consumption. Preventative and rehabilitative measures are discussed. (97 refs)

340. TOBACCO. (PP. 131-138)

Hammond EC
Persons at High Risk of Cancer, an Approach to Cancer Etiology and Control. Fraumeni Jr. JF, ed. New York, Academic Press, Inc. 554 pp., 1975.

Selected aspects of tobacco-related cancer are reviewed and areas for future study suggested. A prospective epidemiological study of over one million men and women between October 1959 and September 1965 gave findings consistent with dozens of other studies. That is, cigarette smoking increases the risk of lung cancer to a greater degree than any other cancer site, multiplies the risk of cancer of the buccal cavity and pharynx by a factor of about 3-10, and increases the risk of cancers of the larynx, esophagus, bladder, and pancreas. Heavy alcohol consumption increases the risk of mouth and throat cancer even further in smokers. Lung cancer death rates increase with the amount of cigarette smoking and with depth of inhalation and are far higher among people who started smoking in their early teens. Men with a lifetime history of only pipe or cigar smoking have a significantly higher lung cancer death rate than men who never smoked, but a considerably lower rate than men who smoked even a few cigarettes a day. This is explained by the fact that most pipe and cigar smokers do not inhale, while most cigarette smokers do. Lung cancer death rates are lower among ex-cigarette smokers than those who continue the habit and are lower among those who have not smoked for many years than those who have not smoked for a few years. Further research should be aimed at the following two questions: (a) does reduction in the tar and/or nicotine content of cigarettes significantly reduce the risk of cancer; and (b) is there an accompanying decrease or increase in the risk of death from other serious diseases, especially coronary heart disease. Preliminary evidence suggests that tar and nicotine in cigarette smoke are mainly responsible for the cancer-producing effects and that reduced exposure can lower the risk of cancer among people who were heavily exposed for many years. Death rates from coronary heart disease, however, were a little higher in men who smoked low tar and nicotine cigarettes than in men who smoked high tar and nicotine cigarettes. This finding may be due to biasing factors that need to be evaluated.

341. TOBACCO AND TOBACCO SMOKE.

Wynder EL, Hoffmann D
American Health Foundation, 1370 Avenue of the Americas, New York, N.Y. 10019
Semin Oncol; 3(1):5-15 1976

The current evidence linking tobacco use to various types of cancers and efforts toward the reduction of these cancers are reviewed. The incidence of tobacco-related cancers is lower in women than in men; however, these differences decrease as the number of women smokers increases. Cigarette smokers have higher risks of cancer of the lungs, pancreas, kidney, and urinary bladder, than do pipe, and cigar smokers, who have higher incidences of cancers of the oral cavity, larynx, and esophagus. Dose responses between number of cigarettes smoked and cancer of the respiratory and upper digestive tracts are reviewed. Experimental evidence identifying tumor initiators and promoters, cocarcinogens, and organ specific carcinogens are discussed. The authors conclude that tobacco-related cancers will be reduced to a greater extent by production of less harmful smoking products than by modification of smokers' behavior. The reduction of tar and nicotine contents in smoking products has reduced the incidences of tobacco-related cancers in animals. Group therapy, individual counseling, and hypnosis are discussed as methods for behavior modification. Recidivism rates were high in all methods; however, group therapy was the most effective method of producing exsmokers. Except in the case of college-educated males, education programs have had little success in producing nonsmokers and exsmokers.

342. SMOKING AND OCCUPATIONAL CANCERS.

Hoffmann D, Wynder EL
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY 10595
Prev Med; 5(2):245-261 1976

Epidemiological evidence that tobacco use has an added effect to that of occupational carcinogens is reviewed. There is a lack of epidemiological data for the joint reaction of occupational carcinogens and tobacco smoke. This applies particularly to workers in nickel refineries, coke oven and gas workers, and for workers in the chemical industries related to halo ethers and vinyl chloride and certain urinary carcinogens. Synergistic and/or additive effects of occupational carcinogens and tobacco smoke are epidemiologically established in the areas of exposure to radon daughters and to some types of asbestos. Experimental evidence of syncarcinogenic and/or cocarcinogenic effects of tobacco smoke and occupational carcinogens is needed in the areas of carcinogenesis of nickel, chromium, arsenicals, vinyl chloride, and halo ethers. The latter, however, are very potent respiratory carcinogens by themselves. Similarly, the aromatic amines as potent industrial bladder carcinogens may be studied for cocarcinogenic mechanisms with tobacco smoke constituents. Epidemiological studies in occupational cancer must include the smoking histories in order to determine the relative contribution of causative factors. Furthermore, it is the heavy cigarette smoker who is most likely to be the first affected by traces of carcinogens. (105 refs)

343. THE HEALTH MENACE OF TOBACCO.

Ochsner A
Ochsner Clin., New Orleans, La.
Am Sci; 59(2):246-252 1971

The epidemiological evidence establishing a causal connection between tobacco use and cancer is reviewed. The increase in mortality from lung cancer in the United States between 1930 (2,500 deaths) and 1964 (43,100 deaths) appears to be related to the fact that cigarette smoking did not become a widespread practice in the United States until the time of the First World War. Statistics from Iceland show that lung cancer mortality began to increase in that country around 1955, and that cigarette smoking became prevalent in Iceland during the Second World War. Adenocarcinoma of the lungs does not appear to be associated with smoking. It also appears that the chance of developing cancer decreases among those who stop smoking, the decrease accompanying the time elapsing since cessation of smoking. Other cancers caused by smoking include laryngeal cancer which is also on the rise in the United States, lip, tongue and oral cancer, esophageal cancer and cancer of the urinary bladder. Bladder cancer is thought to be caused by cigarette smoke interfering with metabolism in such a way as to promote the excretion of carcinogens in the urine.

344. RESEARCH ON SMOKING BEHAVIOR.

NatlInstDrug Abuse
Div. Res., 5600 Fishers Lane, Rockville, MD, 20857
Natl Inst Drug Abuse Res Monogr Ser; (17):230-280 1977

The history and biological effects of smoking tobacco are extensively reveiwed. After a discussion of possible mechanisms of carcinogenesis by tobacco, methods for reducing this carcinogenesis are reviewed.

345. IMPACT OF NEW SMOKING TRENDS ON WOMEN'S OCCUPATIONAL HEALTH.

Mushinski MH, Stellman SD
Div. Epidemiology, American Health Foundation, 320 E. 43rd St., New York, NY, 10017
Prev Med; 7(3):349-365 1978

Health problems related to cigarette smoking, understanding and knowledge of health risks, and specific diseases and occupations presenting major health problems in women are examined. The adverse effects of smoking, synergistic effects with other carcinogens, and enhanced risk of cancer are discussed in relation to women's smoking habits. A dose-response relationship between tobacco-related cancers and type of cigarettes smoked, enhancement of the carcinogenic effect of cigarettes by alcohol consumption, smoking and increased cardiovascular disease risk, smoking and increased incidence of birth defects and pregnancy complications, and smoking and asbestos exposure are evaluated. The carcinogenic action of tobacco smoke, either in association with various inorganic arsenicals or alone, is discussed. A profile of a female smoker is given; smoking trends in women and men are analyzed. Selected demographic characteristics of women by tobacco exposure are tabulated. Occupational hazards encountered by women, including known reproductive hazards, the hazards of the office worker, and exposure to smoke from other's cigarettes while at work are discussed. Future clinical and epidemiological studies focusing on women's occupations are recommended. Epidemiologic variables to be included in studies of occupational health among women workers are suggested. (69 Refs)

346. CIGARETTE SMOKING (A BIBLIOGRAPHY WITH ABSTRACTS).

Harrison EA
Natl. Technical Information Service, Springfield, VA
Cigarette Smoking (A Bibliography with Abstracts). Available Through National Technical Information Service, Springfield, Va., as NTIS/PS-79/0114/3GA:, NTIS/PS-79/0144, 163 pp., 1979.

The selected abstracts of research reports cover coronary artery disease, visual perception, air pollution, respiratory diseases, attitudes, and physiological effects as related to cigarette smoking. (Author abstract)

347. CIGARETTE SMOKING - DOES IT CARRY A GENETIC RISK?

Bridges BA, Clemmesen J, Sugimura T
Medical-Biological Lab. TNO, P.O. Box 45,, 2280 AA Rijswijk, Netherlands
Mutat Res; 65(1):71-81 1979

The possibility of a genetic risk associated with cigarette smoking is reviewed. Evidence indicates that cigarette smoke contains many mutagens and that persons who inhale the smoke probably absorb significant quantities. At least some of the mutagens are distributed systematically and are likely to reach the gonads. Three investigations suggest the existence of genetic damage to the circulating lymphocytes and spermatozoa of smokers. The only available study of heritable effects in man indicated a significant correlation between paternal smoking and both the rate of perinatal mortality and the frequency of congenital abnormalities. It is hypothesized that cigarette smoking may prove to be a significant genetic hazard for the offspring of smokers and for subsequent generations. (34 Refs)

348. ENVIRONMENTAL CARCINOGENESIS.

Wynder EL
Dept. Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
Clin Bull; 8(1):3-9 1978

The role of tobacco, alcohol, and diet in cancer induction is discussed, and measures to prevent environmental carcinogenesis are outlined. (46 Refs)

349. ENVIRONMENTAL CANCER: ON THE CAUSES OF THE MAIN HUMAN CANCERS.

Weisburger JH
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Tex Rep Biol Med; 37:1-20 1978

Causes of the main human cancers are reviewed briefly. Occupationally incurred cancer arises in individuals exposed at work to varied carcinogenic chemicals, and it develops cancer at a site that is determined by the nature of the carcinogen. In the context of the total incidence of cancer in the US, occupational cancer assumes a minor quantitative role. Nonetheless, provided proper plant design and hygienic measures are developed, these cancers are totally preventable. Most of the remaining human cancers US such as cancer of the respiratory and digestive tracts (including the stomach and large bowel) and of the endocrine-sensitive organs (including the breast, prostate, ovary, and endometrium), are related to lifestyle; namely, cigarette smoking and diet. The mechanism whereby lifestyle translates to certain of these diseases is presented. (66 Refs)

350. THE ETIOLOGY OF CANCER.

Wynder EL
no affiliation given
Semin Oncol; 3(1):1 1976

Tobacco usage, alcohol consumption, nutritional factors, radiation and occupational exposure are important in the etiology of cancer. The investigation of these factors may decrease or prevent the incidence of the disease long before the mechanisms are fully understood.

351. NEW EVIDENCE CONCERNING SMOKING AND HEALTH.

Sterling TD
Computing Science Program, Simon Fraser Univ., Burnaby, British Columbia, Canada V5A 1S6
Med J Aust; 2(16):538-542 1977

Knowledge of the impact of airborne substances on human health has increased in the last 20 yr, especially as a result of smoking and health studies. Many sources of toxic and carcinogenic agents in air have been identified. New evidence shows the existence of a complex relationship for exposure from many sources of community pollutants as a result of occupation, smoking, and other personal habits. These pollutants, especially those encountered in blue collar occupations, account for a far larger proportion of cancers of the lung and of other sites than has been thought to be the case. (40 Refs)

352. SMOKING AND CANCER: A REBUTTAL.

Weiss W
Hahnemann Medical Coll., Philadelphia, Pa. 19102
Am J Public Health; 65(9):954-955 1975

Researcher Dr. Theodore Sterling sought to invalidate the cigarette smoking-lung cancer hypothesis by criticizing prospective epidemiologic studies on the grounds of population selection. He particularly singled out the American Cancer Society's investigation of more than 1 million people for criticism, suggesting that the population was loaded with smokers who developed lung cancer and nonsmokers who did not. This presumes remarkable perspicacity among the workers who recruited the population. Moreover, Dr. Sterling omitted reference to several prospective studies, such as the Philadelphia Pulmonary Neoplasm Research Project, which screened populations with periodic chest roentgenograms so that prevalence cases were readily separated from the incidence cases without altering the strong association between cigarette smoking and lung cancer risk. Dr. Sterling is also criticized for using the preliminary 15-mo report of the Japanese study by Hirayama and ignoring the 5-yr results of this prospective study. The data do not confirm Dr. Sterling's contention that the mortality rates of smokers and nonsmokers are largely the same. The ratio of observed deaths expected from the rates in nonsmokers was 1.06 for males and 1.17 for females even in the 15-mo period. The ratio for lung cancer was 2.92. This was exceeded only by the ratios for cancer of the pancreas and cancer of the bladder, and in the 5-yr period these ratios were lower than that for lung cancer. Evidence is also presented that is in disagreement with Dr. Sterling's contention that lung cancer mortality rates are leveling off, and that a constant difference persists between men and women in the incidence of lung cancer despite a more rapid increase in the frequency of smoking among women. Based on clinical, autopsy, experimental, and epidemiological data, the association between smoking and lung cancer is consistent and specific. Recognition of this factor is essential for disease prevention and control.

353. OUR DAILY HABITS AND CANCER.

Werko L
Farmacevtisk Divisionen, Astra Lakemedel AB, Sweden
Lakartidningen; 75(10):919-920 1978

The risk of cancer is increased by tobacco, alcohol, and dietary habits. Positive correlations have been found between alcohol consumption and laryngeal and buccal cavity cancer and between high-fat diets and leukemia or colon and breast cancer. (11 Refs)

354. PERSONAL HABITS.

Wynder EL
American Health Foundation, 1370 Ave. of the Americas, New York, NY, 10019
Bull NY Acad Med; 54(4):397-412 1978

A review of the association between various personal habits and cancer is presented. Among the relationships discussed are the following: tobacco smoking and lung cancer; alcohol intake and cancer of the mouth, esophagus, and larynx; iodine deficiency and cancer of the thyroid; atrophic gastritis and stomach cancer; and fat intake and colon and breast cancer.

355. INTERDISCIPLINARY AND EXPERIMENTAL APPROACHES: METABOLIC EPIDEMIOLOGY. (PP. 485-501)

Wynder EL, Hoffmann D, Chan P, Reddy B
Persons at High Risk of Cancer, an Approach to Cancer Etiology and Control. Fraumeni Jr. JF, ed. New York, Academic Press, Inc, 554 pp., 1975.

The application of the multidisciplinary approach to the study of cancers of the upper alimentary and respiratory tracts and to cancer of the colon is illustrated. Epidemiologic investigations have indicated that cancer of the oral cavity, larynx, and esophagus are uniform throughout the Western world; that cigarettes, pipe tobacco, cigars, and chewing tobacco represent the principal stimulus for development; and that this stimulus is magnified by heavy alcohol consumption. A variety of tumor initiators, promoters, and accelerators in tobacco smoke have been identified, leading to the development of cigarettes having a lower carcinogenic activity than those of 25 yr ago. Alcoholism, iron deficiency, and riboflavin deficiency may have a common denominator during carcinogenesis in that they affect the activity of one of the respiratory enzymes, aryl hydrocarbon hydroxylase, which may be responsible for expressing the carcinogenic effects of polycyclic hydrocarbons. Epidemiologic studies of colon cancer indicated that it is more prevalent in the Western world, its sex ratio is near unity, its worldwide distribution is different from that of cancer of the lower rectum, its incidence is higher in the first and second generations of Japanese migrants to Hawaii and California than in Japan, and that a close correlation exists between its incidence and total fat consumption. Metabolic epidemiology supports the hypothesis that populations on a mixed Western diet, among whom the rate of large-bowel cancer is high, degrade and excrete cholesterol and bile acid metabolites to a greater degree than those populations in which the rate of colon cancer is relatively low. A number of animal studies are in progress to determine whether the quality and quantity of dietary fat and protein as well as intestinal microflora can influence the susceptibility of colon tissues to chemical carcinogens.

356. GEOGRAPHICAL PATHOLOGY IN ENVIRONMENTAL CARCINOGENESIS. (PP. 48-57)

Higginson J
Proceedings of the Eleventh Canadian Cancer Research Conference. Natl Cancer Inst Canada Toronto Ontario 6-8 May 1976, 1976.

The causes of a considerable number of human cancers, including 20%-50% of all cancers among North American and European men, have now been identified by epidemiological investigations of general populations and high risk groups. The incidences of particular cancers at different geographical locations are listed. This information, together with data from migrant studies indicating that cancer patterns tend to approximate those of the host country, suggest that 70%-90% of all cancers are related to environmental factors. Cancers of the lung, esophagus, upper respiratory system, and mouth are associated with cultural habits such as cigarette smoking, excessive alcohol consumption, and betel quid chewing. Cancers of the esophagus, gastrointestinal tract, lung, breast, prostate, and genitourinary system are influenced by migration, and are therefore probably caused by as yet unidentified environmental stimuli. Cancers of the bone and soft tissue and of the hematopoietic system, and childhood neoplasms, tend to show only small geographical variations in incidence: it is among this group that oncogenic viruses are believed most likely to be of importance. The proportion of all cancers due to defined hereditary factors is small; the exceptions are nasopharyngeal cancer, for which a high frequency is observed in overseas Chinese, and retinoblastoma and xeroderma pigmentosum. Epidemiological data alone can provide the accurate evaluation of environmental carcinogenic risks in man that is essential for the control of existing cancer hazards. A system should be established to provide epidemiological data on a global scale.

357. CANCER IN ITS GEOGRAPHICAL PERSPECTIVE (MEETING ABSTRACT).

Doll R, Hutt MS, Jussawalla DJ, Burkitt DP, Higginson J
Radcliffe Infirmary, Oxford, England
Proc R Soc Med; 66(4):307-318 1973

Geographical environment, socio economic or cultural influences on the basic patterns and incidence of cancer are reviewed. In India the upper digestive tract (oral cavity, pharynx and esophagus) and the uterine cervix are most frequently affected. Chewing of pan quid (betel leaves) is an important factor in initiating oral cancer, whereas smoking tends to lead to pharyngeal cancers. Multiple pregnancies starting from an early age represent an important risk factor in those Indian women who ultimately develop cervical cancer. Tobacco plays an important role in the etiology of esophageal cancer in India. A link between alcohol and esophageal cancer is apparent only in association with other factors such as smoking and chewing of tobacco. The site distribution of cancer in India is almost at complete variation with the distribution seen in the West. In Africa cancers of the lung, colon, rectum, body of the uterus and breast have a low frequency while cancers of the liver, cervix and choriocarcinoma have a higher frequency than in Europe. Burkitt's lymphoma and epithelioma, which arises in the often healed scars of tropical leg ulcers, are prevalent exclusively in equatorial countries. Stomach cancer, Kaposi's sarcoma and esophageal cancer exhibit foci of occurrence within East Africa, the latter two being much less prevalent in West Africa. Within East Africa distribution of Burkitt's lymphoma is related to temperature, rain, and the distribution of hyperendemic malaria. The distribution of penile cancer is strongly influenced by circumcision habits, although variations are shown between tribes who do not practice circumcision. In conclusion, the general benefits, potential developments, and limitations of geographical pathology are reviewed. Epidemiological studies could clarify areas of chemical carcinogenesis and be of value in separating and identifying risks. The author previously cited evidence that 80% of tumors in North America and Europe are conditioned by the present environment and thus are theoretically preventable.

358. AN EPIDEMIOLOGICAL PERSPECTIVE OF THE BIOLOGY OF CANCER.

Doll R
Univ. Oxford, Oxford, England
Cancer Res; 38(11,part1):3573-3583 1978

Cancer epidemiology data are reviewed to determine if they can contribute to defining a mechanism of carcinogenesis. There is no evidence for genetic susceptibility to cancer as a whole, but there are differences in susceptibility to individual types of cancer. Epidemiological evidence suggests a possible role for an infectious viral agent in African Burkitt's lymphoma, Hodgkin's disease, cervical cancer, and reticulosarcomas. The incidence of several types of cancer increases after 2 yr of treatment with immunosuppressive drugs. The incidence of leukemia and lymphoreticular tumors is much greater in patients with certain immunodeficiency syndromes than in normal persons, but it is not clear whether the cancers are caused by the immunodeficiency or are associated with it because of a common cause. Susceptibility to radiation-induced cancer increases with age, perhaps as a result of a progressive breakdown in the efficiency of immunosurveillance with age. Studies on tobacco smoking and lung cancer incidence indicate that the incidence increases with duration of exposure and dose, independently of age. The trend in smokers who stop smoking shows an initial fall in incidence followed by an increase, which keeps the rate ahead of that in lifelong nonsmokers. The simplest explanation for these data is that cancer production is a multistage process and that the various stages represent a series of discrete cellular changes that cumulatively result in the production of a malignant clone. (45 Refs)

359. INTERPRETATIONS OF EPIDEMIOLOGIC DATA.

Doll R
University Coll. Hosp. Sch. Med., Gower St., London
Cancer Res; 23(10):1613-1623 1963

A discussion and review on the possible contribution that epidemiology can make to the study of mechanism of carcinogenesis. Examples included the observation that, after a single exposure to radiation, the incidence of leukemia rapidly rises to a max and falls slowly; this may indicate that cancers showing similar distribution with age are also due to brief periods of exposure to the agent concerned. Also noted was the fact that prolonged exposure, as occurs with cigarette smoke, gives rise to a continuous increase in incidence which is similar to that seen with most of the common epithelial cancers, i.e, an incidence which increases approx in proportion to the sixth power of the age. Data was obtained showing the relationship between exposure of epithelial tissue and resulting incidence, and the effect of cessation of exposure and of starting exposure at different ages.

360. EPIDEMIOLOGICAL BASES FOR PRIMARY PREVENTION OF CANCER.

Berndt H
Klinik fur Innere Medizin, Bezirkskrankenhaus, PSF 480, DDR-20 Neubrandenburg, E. Germany
Dtsch Gesundheitsw; 32(52):2449-2453 1977

Epidemiological data are presented on the major human cancers and on the environmental and endogenous factors that may facilitate or prevent them. An unbalanced diet, abuse of tobacco and alcohol usage, sexual promiscuity, and excessive sunbathing are among the factors facilitating the development of certain cancers in humans. (35 Refs)

361. EPIDEMIOLOGICAL IDENTIFICATION OF CANCER HAZARDS (MEETING ABSTRACT). (PP. 1)

Muir CS
Unit of Epidemiology and Biostatistics, International Agency for Research on Cancer, 150, cours Albert Thomas, 69008 Lyon, France
Third International Symposium On Detection And Prevention Of Cancer. 1976.

There are many avenues to the identification of cancer hazards. Consideration of routinely collected data on the histological type and geographical distribution may point to possible causal factors, as may changes in risk following migration, and clinical observation. Hypotheses may emerge from correlation studies comparing the distribution of environmental factors with that of cancer. The validity of hypotheses so elaborated is usually tested by case/control studies, often in a variety of situations to see if the results are consistent. Prospective studies of well-defined groups have uncovered risks associated with occupation or with a variety of habits and exposures. By its very nature the epidemiological approach permits assessment of the risk for a group, not for an individual in that group. Many cancers are likely to be multifactorial in origin, yet epidemiological techniques to examine such interactions are largely lacking. There is good reason to believe that the majority of human cancers are of environmental origin. The risk factors hitherto uncovered by epidemiological methods seem to be of two types: (a) very powerful carcinogens acting on a relatively small group of workers. Such exposures can be controlled by legislation. The significance of low levels of exposure to such agents of the general public often remains to be assessed. (b) widely distributed agents, which account for very large numbers of cancers, such as smoking, excessive alcohol consumption, and perhaps diet, over which there is a large measure of personal control. (Author Abstract)

362. EPIDEMIOLOGICAL IDENTIFICATION OF CANCER HAZARDS. (PP. 3-23)

Muir CS
Unit Epidemiology and Biostatistics, International Agency Res. Cancer, Lyons, France
Prevention and Detection of Cancer. Part II. Detection. Vol. 1. High Risk Markers. Detection Methods and Management. Nieburgs HE, ed. New York, Marcel Dekker, 1299 pp., 1978.

Epidemiologic approaches to the identification of cancer hazards are reviewed. As a basis on which to formulate hypotheses, the epidemiologist can examine the behavior of the disease itself with regard to age and sex patterns, geographical distribution between and within countries, variations in histologic type, changes over time and in migrant populations, and clinical observations. These data can then be used to formulate a hypothesis that can be tested by epidemiologic techniques, including case/control and prospective studies. Examples of these techniques are presented. The results of epidemiologic studies have shown that the majority of human cancers are probably due to environmental agents, acting singly or in combination. These agents are of two major types: powerful carcinogens acting on a relatively small number of workers and with generally unknown significance for the general population; and widely distributed agents such as tobacco smoke and excessive exposure to sunlight, over which there is a large measure of personal control. With regard to prevention of carcinogenesis by these agents, much has to be done by the government to protect worker and community. (37 Refs)

363. IDENTIFICATION OF TUMOR SUSCEPTIBILITY OF INDIVIDUALS AT HIGH RISK FOR THE DEVELOPMENT OF CANCER. (PP. 1493-1512)

Rawson RW
Univ. Texas System Cancer Center, Houston, TX
Prevention and Detection of Cancer. Part I. Prevention. Vol. 2. Etiology-Prevention Methods. Proceedings of the Third International Symposium on Detection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 2402 pp., 1978.

Factors that can identify high-cancer-risk individuals and/or populations are reviewed, and they include host or intrinsic factors (genetic, congenital, and immune deficiency disorders, acquired nonneoplastic diseases, previous cancers), environmental factors (demographic, geographic, occupational, radiation, air pollution, viruses), and individual living patterns (tobacco, alcohol, diet, drugs, sexual practices). (76 Refs)

364. AETIOLOGICAL FACTORS IN HUMAN CANCER.

Higginson J, MacLennan R, Muir CS
The Physiology of Cancer. Homburger F, Brennen MJ, Krakoff IH, ed. Basel, S Karger, vol. 2, 1976.

The precise etiology of 90% of human cancers is unknown but for practical prevention cancers may be classified in broad groups according to the suspected agent or type of exposure. Three types of agents (physical, chemical, and viral) and three types of exposure (cultural, occupational, and iatrogenic) are considered briefly. The role of genetic factors in cancer etiology is generally unknown. Most oral cancer is associated with either the use of tobacco or heavy spirit drinking. Genetic factors appear to play a role in nasopharyngeal cancer in men - it has a very high incidence in Southern Chinese and in their descendants who have migrated. There appear to be two major groups of esophageal cancer with regard to etiology: one is associated with high consumption of strong alcohol and the other with exposure to nitrosamines. Current evidence suggests the importance of environmental factors in cancer of the stomach, colon, and rectum. Liver cancer has been associated with alcoholic cirrhosis, with ingestion of aflatoxin, and with hepatitis B antigen. The possibility that bile may contain carcinogens or their precursors is being studied in relation to cancer of the gallbladder and the extrahepatic biliary ducts, the pancreas, and the large intestine. Most sinus cancers are associated with occupational hazards, except for those in South African blacks; these are associated with the use of snuffs containing powdered aloes, tobacco, chromium, and nickel. Laryngeal and lung cancer are closely connected with cigarette smoking; lung cancer is also associated with asbestos and ionizing radiation. Breast cancer risk increases with the age at which a woman bears her first full-term child. Cancer of the cervix appears to be directly related to sexual intercourse, since it is rare in nuns and frequent in prostitutes. The etiology of cancer of the prostate, testis, and penis is unknown. There is a small increase in risk for kidney cancer in cigarette smokers and also an association with excessive use of phenacetin containing analgesics. Cigarette smoking is the most important risk factor for bladder cancer; 10%-20% of male bladder cancer in Western Europe is due to occupational exposure. Exposures to sunlight and arsenic are important etiological factors in skin cancer. Etiological factors associated with leukemia include chemical agents, such as benzene, and irradiation in various forms. (62 refs)

365. ON THE ETIOLOGY AND METABOLIC EPIDEMIOLOGY OF THE MAIN HUMAN CANCERS. (PP. 567-602)

Weisburger JH, Cohen LA, Wynder EL
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Incidence of Cancer in Humans, Proceedings of the Cold Spring Harbor Conferences on Cell Proliferation. Vol. 4, Hiatt HH, Watson JD, Winsten JA, ed. Cold Spring Harbor, Cold Spring Harbor Laboratory, Origins of Human Cancer., 602 pp., 1977.

Concepts maintaining that the etiologies of the main human cancers stem largely from human life-styles are reviewed. Most cancers of the respiratory tract are due to excessive smoking, as are cancers of the pancreas, kidneys, and bladder. Prevention of these diseases hinges on education of the public and collaboration of industry and government to produce and give preferential marketing to lower tar cigarettes. Cancers of the breast, prostate, ovary, endometrium, and colon are associated with a high fat content in the diet. Cancer of the pancreas is also associated in part with diet. Prevention of these cancers hinges on lowering fat consumption from the prevailing level of 45% of the caloric intake to 25%-33%. This would be aided by cooperation of industry with agricultural and governmental agencies to produce and market foodstuffs that would permit the consumer to adopt the lower fat diet more readily or automatically. Cancer of the stomach might be prevented by increasing the consumption of vitamin C, low-temperature food storage to prevent nitrite formation, and controlling the use of nitrite as a preservative. (155 Refs)

366. CURRENT VIEWS ON MECHANISMS CONCERNED WITH THE ETIOLOGY OF CANCERS IN THE DIGESTIVE TRACT. (PP. 1-20)

Weisburger JH
Naylor Dana Inst. Disease Prevention, American Health Foundation, Valhalla, NY
Pathophysiology of Carcinogenesis in Digestive Organs Proceedings of the 7th International Symposium of The Princess Takamatsu Cancer Research Fund, Tokyo, 1976 The Princess Takamatsu Cancer Research Fund, Tokyo, Japan, 441 pp., 1977.

The etiology of cancer of the digestive organs is discussed. In the past 40 yr, an increase in fat intake in the US has been accompanied by an increase in colon cancer. Furthermore, bacteria that produce secondary bile acids are present in higher quantities in the stools of high-risk subjects than in those of low-risk subjects. Parallel results were obtained in animal studies, in which it was also shown that bile acids have a promotional effect on colon cancer in conventional and germ-free animals. This suggests that these acids are involved in human colonic cancer. An association has also been postulated among diet, smoking, and pancreatic cancer. As with colonic cancer, it is fat intake in the diet that is implicated. Examination of gastric cancer indicates that nitrite-containing foods appear to have an etiological role. These nitrites are either added as preservatives or they are from foods grown in soil with high nitrite levels. Furthermore, populations at risk for gastric cancer usually eat a diet containing high levels of carbohydrates and salts, and limited micronutrients, especially vitamin C. Vitamin C has been shown to prevent mutagen formation from nitrite under similar human gastric conditions. It may also prevent the formation of carcinogenic alkylnitrosamides from nitrites.

367. DIETARY HABITS AND CANCER EPIDEMIOLOGY.

Wynder EL
American Health Foundation, 320 E. 43rd Street, New York, NY, 10017
Cancer; 43(5,Suppl):1955-1961 1979

The hypothesis that specific nutritional deficiencies and unbalanced metabolism from dietary excesses are important in the etiology of many of the most common human cancers is reviewed. Alcohol and nutritional deficiencies could enhance carcinogenesis in tobacco smokers by increasing the microsomal metabolic activation of specific tobacco carcinogens. It appears to be fat and/or cholesterol in the diet which is primarily responsible for the association between diet and colon cancer. Bile acid production appears to be particularly important in colon carcinogenesis, and stool bulk may be a negative modifying factor. The fact that Finns ingest large amounts of dietary fat but have low rates of colon cancer indicates that total fat alone is not the only factor in colon carcinogenesis, however. Breast cancer also appeared to be associated with dietary fat, particularly animal fat. High rates of postmenopausal cancers may be due to increased prolactin/estrogen ratios. (58 Refs)

368. NUTRITION AND ALIMENTARY CANCER (MEETING ABSTRACT). (P. 16)

Hirayama T
Epidemiology Div., Natl. Cancer Res. Inst., Tokyo, Japan
National Cancer Week, Proceedings of the Australian Symposium on Nutrition and Cancer held in Adelaide, Australia, 20-24 November 1978. South Australian Postgraduate Medical Education Association Incorporated, 175 pp., 1978.

Different distribution of cancers in various parts of the world, in various ethnic groups, in different socioeconomic strata and changing risk in migrants clearly indicate the possible influence of diet and nutrition. There is epidemiological and laboratory evidence to support the view that diet and nutrition have a profound influence on the risk and pathogenesis of a great variety of human cancers, in particular of alimentary organs. In this regard, correlation studies, case control studies and prospective studies were all proved to be useful. Qualitative and quantitative aspects of such relationships and mechanisms should be explored intensively by a multidisciplinary task force. Operational epidemiology is of key importance in dietary strategy of cancer control. Diet, smoking and drinking are strongly integrated into life styles, customs, and habits of people. Sometimes it even becomes a part of chronobiology of individuals which governs types, patterns, and cycles of enzymes and other key biological substances. A special effort appears to be necessary to develop behavioral science and market research to manipulate dietary habits. Another approach is dietary engineering. The impressive reduction of cancer of the upper alimentary tract in Swedish women through iron vitamin enriched breads must indicate one of the directions we should follow. Innovative research on operational aspects of diet and cancer should actively be promoted to minimize risks of the disease while maximizing our pleasure in dietary life. (no Refs)

369. CHANGING PATTERNS OF CANCER.

Anonymous
Br Med J; 1(6005):301-302 1976

Information obtained from various cancer registries is presented. In a British series of 1,478 cases of carcinoma of the bronchus from 1950 to 1970 the peak age was 56-60 in the first decade and had risen to 61-65 in the second. The number of persons treated by surgery was lower in the first decade than in the second. The number of men aged 60-69 alive in England and Wales had increased between 1950 and 1970 by 640,000, and it was this group that largely accounted for an increase in lung cancer deaths during this period. Further evidence suggests that a cohort of persons particularly at risk is moving through the population and that as they grow older their probability of presenting with bronchial cancer is increasing until about 70, after which it is fairly static. The most probable environmental factor affecting these people is their smoking habits. A further cohort effect in bladder cancer has been reported in Denmark. The incidence of some cancers, such as pancreatic and ovarian cancers, is increasing; the latter increases by about 15% each decade.

370. ARE 90% OF CANCERS PREVENTABLE?

Anonymous
No affiliation given
Lancet; 1(8013):685-687 1977

The possibility of reducing cancer incidence by 90% by the removal of specific environmental carcinogens is considered. Removal of known carcinogens should lead to a substantial fall in cancer incidence, but with current knowledge the estimate of 90% seems optimistic. In British men the figure is probably closer to 50%-60%. Smoking is responsible for most lung cancers and for a smaller proportion of the cancers of the larynx, pharynx, esophagus, bladder, and pancreas, which together account for almost half the cancers that occur among British men. The elimination of smoking alone could, therefore, almost halve cancer incidence. The proportion of all cancers associated with other known carcinogens is rather small and includes the alcohol-related cancers, such as those of the esophagus and liver, occupational cancers, and iatrogenic cancers. The elimination of all these would probably not reduce the total cancer incidence by 10%. The proportion of cancers that are environmentally determined is greater for men than for women, perhaps because a woman's exposure to the environment is more uniform. These observations suggest that the potential reduction in cancer incidence in women, while still considerable, is not of the same order of magnitude as that predicted in men. If cancer is to be prevented, changes in behavior, diet, alcohol consumption, and smoking will be necessary. (17 Refs)

371. ENVIRONMENTAL FACTORS AND CANCER PREVENTION. (PP. 1867-1877)

Schneiderman MA
Field Studies and Statistics Program, Div. Cancer Cause and Prevention, NCI, Bethesda, MD, 20014
Prevention and Detection of Cancer. Part I. Prevention. Vol. 2. Etiology-Prevention Methods. Proceedings of the Third International Symposium on Detection and Prevention of Cancer held 26 April - 1 May 1976 New York NY. Nieburgs HE, ed.New York, Marcel Dekker, Inc., 2402 pp., 1978.

Environmental factors and cancer prevention are discussed in terms of relative risk and proportion of the general population exposed. Estimates are presented of the attributable risk, expected deaths and preventable deaths using 1976 data from the United States. The sites and suggested controllable factors are tabulated. Cancers of the lung, larynx, and other respiratory sites can be reduced through control of cigarette smoking, occupational exposures, and urban pollutants. Cancers of the oral cavity, head, neck, and esophagus can be reduced through control of cigarette smoking and high alcohol intake. Cancers of the bladder and liver can be reduced through control of cigarette smoking, industrial exposure and alcohol intake, and so on. Cancers of the colon and rectum, pancreas, breast, skin, and uterine cervix are also discussed. The diseases listed contributed to approx 236,700 deaths, and an estimate of preventable deaths is a little more than half of that. Some of the factors contributing to the cause of these cancers cannot be interfered with, and a number of interactions of factors in the causation of cancer have not been specifically examined. The use of the attributable risk measure for the computation of possible savings and for effective health planning is discussed. (13 Refs)

372. EIGHTY PERCENT OF CANCER IS RELATED TO THE ENVIRONMENT.

Schneiderman MA
NCI, Landow Bldg., Room C403, Bethesda, MD, 20014
Laryngoscope; 88(4):559-574 1978

A review of epidemiologic data on cancer incidence suggests that as much as 80% of all cancers are related to environmental factors. These factors include personal variables such as cigarette smoking, alcohol consumption, sexual habits, and diet and impersonal variables such as industrial and occupational pollutants, water and air contaminants, pesticides, flame retardants, diet additives, and drugs. Elimination or reduction of these environmental factors would bring about a significant decline in cancer mortality. (18 Refs)

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Chemistry and "In Vitro Bioassay" of Smoke from Experimental Filter Cigarettes. DHEW, Publication No. (NIH) 76-1076, 42 pp., 1976.

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